INVENTOR SEARCH

=> fil capl; d que l22; fil medl; d que l43; fil embase; d que l65; fil wpix; d que l88; dup rem l43,l22,l88,l65
FILE 'CAPLUS' ENTERED AT 14:49:01 ON 20 SEP 2007
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FILE COVERS 1907 - 20 Sep 2007 VOL 147 ISS 13
FILE LAST UPDATED: 19 Sep 2007 (20070919/ED)

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L1	1	SEA FILE=CAPLUS ABB=ON	US2006-567406/AP
L2	608	SEA FILE=CAPLUS ABB=ON	HOLST LANGE B?/AU OR LANGE B?/AU OR HOLST B?/AU
L3	1134	SEA FILE=CAPLUS ABB=ON	HANSEN C?/AU
L4	1	SEA FILE=CAPLUS ABB=ON	COPENHAGEN H?/AU
L5	471	SEA FILE=CAPLUS ABB=ON	NILSSON H?/AU
L7	1	SEA FILE=REGISTRY ABB=ON	304853-26-7
L8	75	SEA FILE=CAPLUS ABB=ON	L7/D
L21	5	SEA FILE=CAPLUS ABB=ON	(L2 OR L3 OR L4 OR L5) AND L8
L22	5	SEA FILE=CAPLUS ABB=ON	(L1 OR L21)

FILE 'MEDLINE' ENTERED AT 14:49:01 ON 20 SEP 2007

FILE LAST UPDATED: 19 Sep 2007 (20070919/UP). FILE COVERS 1950 TO DATE.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L24	471	SEA FILE=MEDLINE ABB=ON	HOLST LANGE B?/AU OR LANGE B?/AU OR HOLST B?/AU
L25	845	SEA FILE=MEDLINE ABB=ON	HANSEN C?/AU
L26	300	SEA FILE=MEDLINE ABB=ON	COPENHAGEN H?/AU OR NILSSON H?/AU
L28	2304	SEA FILE=MEDLINE ABB=ON	GHRELIN
L43	9	SEA FILE=MEDLINE ABB=ON	(L24 OR L25 OR L26) AND L28

FILE 'EMBASE' ENTERED AT 14:49:02 ON 20 SEP 2007

FILE COVERS 1974 TO 20 Sep 2007 (20070920/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L60	2434	SEA FILE=EMBASE ABB=ON	GHRELIN/CT
L61	7	SEA FILE=EMBASE ABB=ON	GHRELIN DERIVATIVE/CT
L62	410	SEA FILE=EMBASE ABB=ON	HOLST LANGE B?/AU OR LANGE B?/AU OR HOLST B?/AU
L63	638	SEA FILE=EMBASE ABB=ON	HANSEN C?/AU
L64	259	SEA FILE=EMBASE ABB=ON	COPENHAGEN H?/AU OR NILSSON H?/AU
L65	8	SEA FILE=EMBASE ABB=ON	(L62 OR L63 OR L64) AND (L60 OR L61)

FILE 'WPIX' ENTERED AT 14:49:02 ON 20 SEP 2007

FILE LAST UPDATED: 14 SEP 2007 <20070914/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE: 200759 <200759/DW>
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'BI ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

L74	191	SEA FILE=WPIX ABB=ON	HOLST LANGE B?/AU OR LANGE B?/AU OR HOLST B?/AU
L75	453	SEA FILE=WPIX ABB=ON	HANSEN C?/AU
L76	157	SEA FILE=WPIX ABB=ON	COPENHAGEN H?/AU OR NILSSON H?/AU
L77	1	SEA FILE=WPIX ABB=ON	L74 AND L75 AND L76
L79	3107	SEA FILE=WPIX ABB=ON	CACHEXIA/BI,ABEX OR CACHECTIC?/BI,ABEX
L80	570	SEA FILE=WPIX ABB=ON	B14-E11B/MC OR C14-E11B/MC
L81	212	SEA FILE=WPIX ABB=ON	GHRELIN/BI,ABEX
L82	542701	SEA FILE=WPIX ABB=ON	ANALOG?/BI,ABEX OR SECRETAGOG?/BI,ABEX

OR DERIVATI?/BI,ABEX
L84 23 SEA FILE=WPIX ABB=ON L81(1A)L82
L87 8 SEA FILE=WPIX ABB=ON (L74 OR L75 OR L76) AND (L84 OR (L81 AND (L79 OR L80)))
L88 8 SEA FILE=WPIX ABB=ON (L87 OR L77)

FILE 'MEDLINE' ENTERED AT 14:49:03 ON 20 SEP 2007

FILE 'CAPLUS' ENTERED AT 14:49:03 ON 20 SEP 2007
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FILE 'WPIX' ENTERED AT 14:49:03 ON 20 SEP 2007

FILE 'EMBASE' ENTERED AT 14:49:03 ON 20 SEP 2007

PROCESSING COMPLETED FOR L43
PROCESSING COMPLETED FOR L22
PROCESSING COMPLETED FOR L88
PROCESSING COMPLETED FOR L65
L90 18 DUP REM L43 L22 L88 L65 (12 DUPLICATES REMOVED)
ANSWERS '1-9' FROM FILE MEDLINE
ANSWERS '10-14' FROM FILE CAPLUS
ANSWERS '15-17' FROM FILE WPIX
ANSWER '18' FROM FILE EMBASE

=> d iall 1-9; d ibib ab hitind 10-14; d iall abeq tech 15-17; d iall 18

L90 ANSWER 1 OF 18 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2007344081 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17371869
TITLE: Identification of an efficacy switch region in the ghrelin receptor responsible for interchange between agonism and inverse agonism.
AUTHOR: Holst Birgitte; Mokrosinski Jacek; Lang Manja; Brandt Erik; Nygaard Rie; Frimurer Thomas M; Beck-Sickinger Annette G; Schwartz Thue W
CORPORATE SOURCE: Laboratory for Molecular Pharmacology, The Panum Institute, Blegdamsvej 3, University of Copenhagen, 2200 Copenhagen N, Denmark.. b.holst@molpharm.dk
SOURCE: The Journal of biological chemistry, (2007 May 25) Vol. 282, No. 21, pp. 15799-811. Electronic Publication: 2007-03-19.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200707
ENTRY DATE: Entered STN: 12 Jun 2007
Last Updated on STN: 19 Jul 2007
Entered Medline: 18 Jul 2007

ABSTRACT:
The carboxyamidated wFwLL peptide was used as a core ligand to probe the structural basis for agonism versus inverse agonism in the constitutively

active ghrelin receptor. In the ligand, an efficacy switch could be built at the N terminus, as exemplified by AwFwLL, which functioned as a high potency agonist, whereas KwFwLL was an equally high potency inverse agonist. The wFw-containing peptides, agonists as well as inverse agonists, were affected by receptor mutations covering the whole main ligand-binding pocket with key interaction sites being an aromatic cluster in transmembrane (TM)-VI and -VII and residues on the opposing face of TM-III. Gain-of-function in respect of either increased agonist or inverse agonist potency or swap between high potency versions of these properties was obtained by substitutions at a number of positions covering a broad area of the binding pocket on TM-III, -IV, and -V. However, in particular, space-generating substitutions at position III:04 shifted the efficacy of the ligands from inverse agonism toward agonism, whereas similar substitutions at position III: 08, one helical turn below, shifted the efficacy from agonism toward inverse agonism. It is suggested that the relative position of the ligand in the binding pocket between this "efficacy shift region" on TM-III and the opposing aromatic cluster on TM-VI and TM-VII leads either to agonism, i.e. in a superficial binding mode, or it leads to inverse agonism, i.e. in a more profound binding mode. This relationship between different binding modes and opposite efficacy is in accordance with the Global Toggle Switch model for 7TM receptor activation.
CONTROLLED TERM: Amino Acid Substitution
Animals
Binding Sites: GE, genetics
COS Cells
Cercopithecus aethiops
Humans
Ligands
*Models, Molecular
Mutation, Missense
*Peptides: CH, chemistry
Peptides: GE, genetics
Protein Binding: GE, genetics
Protein Structure, Secondary
*Receptors, G-Protein-Coupled: AG, agonists
Receptors, G-Protein-Coupled: CH, chemistry
Receptors, G-Protein-Coupled: GE, genetics
Structure-Activity Relationship
CHEMICAL NAME: 0 (Ligands); 0 (Peptides); 0 (Receptors, G-Protein-Coupled); 0 (growth hormone secretagogue receptor)

L90 ANSWER 2 OF 18 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2006740461 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16959833
TITLE: GPR39 signaling is stimulated by zinc ions but not by obestatin.
AUTHOR: Holst Birgitte; Egerod Kristoffer L; Schild Enrico; Vickers Steve P; Cheetham Sharon; Gerlach Lars-Ole; Storjohann Laura; Stidsen Carsten E; Jones Rob; Beck-Sickinger Annette G; Schwartz Thue W
CORPORATE SOURCE: Laboratory for Molecular Pharmacology, The Panum Institute, University of Copenhagen, Blegdamsvej 3, DK-2200 Copenhagen, Denmark.
SOURCE: Endocrinology, (2007 Jan) Vol. 148, No. 1, pp. 13-20. Electronic Publication: 2006-09-07.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200702
ENTRY DATE: Entered STN: 21 Dec 2006
Last Updated on STN: 14 Feb 2007
Entered Medline: 13 Feb 2007

ABSTRACT:
GPR39 is an orphan member of the ghrelin receptor family that recently was suggested to be the receptor for obestatin, a peptide derived from the ghrelin precursor. Here, we compare the effect of obestatin to the effect of Zn(2+) on signal transduction and study the effect of obestatin on food intake. Although Zn(2+) stimulated inositol phosphate turnover, cAMP production, arrestin mobilization, as well as cAMP response element-dependent and serum response element-dependent transcriptional activity in GPR39-expressing cells as opposed to mock-transfected cells, no reproducible effect was obtained with obestatin in the GPR39-expressing cells. Moreover, no specific binding of obestatin could be detected in two different types of GPR39-expressing cells using three different radioiodinated forms of obestatin. By quantitative PCR analysis, GPR39 expression was readily detected in peripheral organs such as duodenum and kidney but not in the pituitary and hypothalamus, i.e. presumed central target organs for obestatin. Obestatin had no significant and reproducible effect on acute food intake in either freely fed or fasted lean mice. It is concluded that GPR39 is probably not the obestatin receptor. In contrast, the potency and efficacy of Zn(2+) in respect of activating signaling indicates that this metal ion could be a physiologically relevant agonist or modulator of GPR39.

CONTROLLED TERM:
Animals
Arrestin: ME, metabolism
CHO Cells
COS Cells
Cercopithecus aethiops
Cricetinae
Cricetulus
Cyclic AMP: ME, metabolism
DNA-Binding Proteins: GE, genetics
DNA-Binding Proteins: ME, metabolism
Eating: DE, drug effects
Gene Expression: PH, physiology
Genes, Reporter
Humans
Inositol Phosphates: ME, metabolism
Integrases: GE, genetics
Kidney: CY, cytology
Luciferases: GE, genetics
Mice
Mice, Inbred C57BL
*Peptide Hormones: ME, metabolism
Peptide Hormones: PD, pharmacology
Polymerase Chain Reaction
Receptors, G-Protein-Coupled: GE, genetics
*Receptors, G-Protein-Coupled: ME, metabolism
Signal Transduction: DE, drug effects
*Signal Transduction: PH, physiology
Transcription Factors: GE, genetics
Transcription Factors: ME, metabolism
Tritium: DU, diagnostic use
*Zinc: ME, metabolism
Zinc: PD, pharmacology

CAS REGISTRY NO.: 10028-17-8 (Tritium); 60-92-4 (Cyclic AMP); 7440-66-6 (Zinc)
CHEMICAL NAME: 0 (Arrestin); 0 (DNA-Binding Proteins); 0 (GPR39 protein, human); 0 (Inositol Phosphates); 0 (Peptide Hormones); 0 (Receptors, G-Protein-Coupled); 0 (SRE protein, human); 0 (Transcription Factors); 0 (obestatin, human); EC 1.13.12.- (Luciferases); EC 2.7.7.- (Cre recombinase); EC 2.7.7.- (Integrases)

L90 ANSWER 3 OF 18 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2006499893 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16798937
TITLE: Ghrelin receptor inverse agonists: identification of an active peptide core and its interaction epitopes on the receptor.
AUTHOR: Holst Birgitte; Lang Manja; Brandt Erik; Bach Anders; Howard Andrew; Frimurer Thomas M; Beck-Sickinger Annette; Schwartz Thue W
CORPORATE SOURCE: Laboratory for Molecular Pharmacology, The Panum Institute, University of Copenhagen, Blegdamsvej 3, DK-2200 Copenhagen, Denmark.. b.holst@molpharm.dk
SOURCE: Molecular pharmacology, (2006 Sep) Vol. 70, No. 3, pp. 936-46. Electronic Publication: 2006-06-23.
Journal code: 0035623. ISSN: 0026-895X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200609
ENTRY DATE: Entered STN: 23 Aug 2006
Last Updated on STN: 29 Sep 2006
Entered Medline: 28 Sep 2006

ABSTRACT:
[D-Arg1,D-Phe5,D-Trp7,9,Leu11]Substance P functions as a low-potency antagonist but a high-potency full inverse agonist on the ghrelin receptor. Through a systematic deletion and substitution analysis of this peptide, the C-terminal carboxyamidated pentapeptide wFwLX was identified as the core structure, which itself displayed relatively low inverse agonist potency. Mutational analysis at 17 selected positions in the main ligand-binding crevice of the ghrelin receptor demonstrated that ghrelin apparently interacts only with residues in the middle part of the pocket (i.e., between transmembrane (TM)-III, TM-VI and TM-VII). In contrast, the inverse agonist peptides bind in a pocket that extends all the way from the extracellular end of TM-II (AspII:20) across between TM-III and TM-VI/VII to TM-V and TM-IV. The potency of the main inverse agonist could be improved up to 20-fold by a number of space-generating mutants located relatively deep in the binding pocket at key positions in TM-III, TM-IV and TM-V. It is proposed that the inverse agonists prevent the spontaneous receptor activation by inserting relatively deeply across the main ligand-binding pocket and sterically blocking the movement of TM-VI and TM-VII into their inward-bend, active conformation. The combined structure-functional analysis of both the ligand and the receptor allowed for the design of a novel, N-terminally Lys-extended analog of wFwLL, which rescued the high-potency, selective inverse agonism that was dependent upon both AspII:20 and GluIII:09. The identified pharmacophore can possibly serve as the basis for targeted discovery of also nonpeptide inverse agonists for the ghrelin receptor.

CONTROLLED TERM:
Amino Acid Sequence
Amino Acid Substitution
Animals
Binding Sites
COS Cells
Cells, Cultured

Cercopithecus aethiops
*Epitopes: ME, metabolism
Humans
Ligands
Models, Molecular
Molecular Sequence Data
Mutant Proteins: AG, agonists
Mutant Proteins: CH, chemistry
Peptide Hormones: ME, metabolism
*Peptides: CH, chemistry
Protein Binding
*Receptors, G-Protein-Coupled: AG, agonists
Receptors, G-Protein-Coupled: CH, chemistry
Structure-Activity Relationship
*Substance P: AA, analogs & derivatives
Substance P: CH, chemistry

CAS REGISTRY NO.: 33507-63-0 (Substance P); 96736-12-8 (substance P, Phe(5)-Trp(7,9)-Leu(11)-)

CHEMICAL NAME: 0 (Epitopes); 0 (Ligands); 0 (Mutant Proteins); 0 (Peptide Hormones); 0 (Peptides); 0 (Receptors, G-Protein-Coupled); 0 (ghrelin); 0 (growth hormone secretagogue receptor)

L90 ANSWER 4 OF 18 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2005456178 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15905359
TITLE: Nonpeptide and peptide growth hormone secretagogues act both as ghrelin receptor agonist and as positive or negative allosteric modulators of ghrelin signaling.
AUTHOR: Holst Birgitte; Brandt Erik; Bach Anders; Heding Anders; Schwartz Thue W
CORPORATE SOURCE: Laboratory for Molecular Pharmacology, Department of Pharmacology, The Panum Institute, Blegdamsvej 3, DK-2200, Copenhagen, Denmark.. b.holst@molpharm.dk
SOURCE: Molecular endocrinology (Baltimore, Md.), (2005 Sep) Vol. 19, No. 9, pp. 2400-11. Electronic Publication: 2005-05-19.
Journal code: 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 27 Aug 2005
Last Updated on STN: 30 Dec 2005
Entered Medline: 29 Dec 2005

ABSTRACT:
Two nonpeptide (L692,429 and MK-677) and two peptide [GH-releasing peptide (GHRP)-6 and ghrelin] agonists were compared in binding and in signal transduction assays: calcium mobilization, inositol phosphate turnover, cAMP-responsive element (CRE), and serum-responsive element (SRE) controlled transcription, as well as arrestin mobilization. MK-677 acted as a simple agonist having an affinity of 6.5 nm and activated all signal transduction systems with similar high potency (0.2-1.4 nm). L-692,429 also displayed a very similar potency in all signaling assays (25-60 nm) but competed with a 1000-fold lower apparent affinity for ghrelin binding and surprisingly acted as a positive allosteric receptor modulator by increasing

ghrelin 's potency 4- to 10-fold. In contrast, the potency of GHRP-6 varied 600-fold (0.1-61 nm) depending on the signal transduction assay, and it acted as a negative allosteric modulator of ghrelin signaling. Unexpectedly, the maximal signaling efficacy for ghrelin was increased above what was observed with the hormone itself during coadministration with the nonendogenous agonists. It is concluded that agonists for the ghrelin receptor vary both in respect of their intrinsic agonist properties and in their ability to modulate ghrelin signaling. A receptor model is presented wherein ghrelin normally only activates one receptor subunit in a dimer and where the smaller nonendogenous agonists bind in the other subunit to act both as coagonists and as either neutral (MK-677), positive (L-692,429), or negative (GHRP-6) modulators of ghrelin function. It is suggested that an optimal drug candidate could be an agonist that also is a positive modulator of ***ghrelin*** signaling.

CONTROLLED TERM: Allosteric Regulation
Amino Acid Sequence
Animals
Arrestin: ME, metabolism
Benzazepines: CH, chemistry
*Benzazepines: PD, pharmacology
CREB-Binding Protein: ME, metabolism
Calcium: ME, metabolism
Humans
Indoles: CH, chemistry
*Indoles: PD, pharmacology
Inositol Phosphates: ME, metabolism
Molecular Sequence Data
Molecular Structure
Oligopeptides: CH, chemistry
*Oligopeptides: PD, pharmacology
Peptide Hormones: CH, chemistry
*Peptide Hormones: PD, pharmacology
*Receptors, G-Protein-Coupled: AG, agonists
Response Elements
Serum Response Element
Signal Transduction
Spiro Compounds: CH, chemistry
*Spiro Compounds: PD, pharmacology
Tetrazoles: CH, chemistry
*Tetrazoles: PD, pharmacology
Transcription, Genetic

CAS REGISTRY NO.: 145455-23-8 (L 692429); 7440-70-2 (Calcium); 87616-84-0 (growth hormone releasing hexapeptide)

CHEMICAL NAME: 0 (Arrestin); 0 (Benzazepines); 0 (CREBBP protein, human); 0 (Indoles); 0 (Inositol Phosphates); 0 (L 163191); 0 (Oligopeptides); 0 (Peptide Hormones); 0 (Receptors, G-Protein-Coupled); 0 (Spiro Compounds); 0 (Tetrazoles); 0 (ghrelin); 0 (growth hormone secretagogue receptor); EC 2.3.1.48 (CREB-Binding Protein)

L90 ANSWER 5 OF 18 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2004643243 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15383539
TITLE: Common structural basis for constitutive activity of the ghrelin receptor family.
AUTHOR: Holst Birgitte; Holliday Nicholas D; Bach Anders; Elling Christian E; Cox Helen M; Schwartz Thue W
CORPORATE SOURCE: Laboratory for Molecular Pharmacology, Department of Pharmacology, The Panum Institute, University of

Copenhagen, Blegdamsvej 3, DK-2200, Copenhagen, Denmark.. b.holst@molpharm.dk
SOURCE: The Journal of biological chemistry, (2004 Dec 17) Vol. 279, No. 51, pp. 53806-17. Electronic Publication: 2004-09-21.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 29 Dec 2004
Last Updated on STN: 5 Feb 2005
Entered Medline: 4 Feb 2005

ABSTRACT:
Three members of the ghrelin receptor family were characterized in parallel: the ghrelin receptor, the neurotensin receptor 2 and the orphan receptor GPR39. In transiently transfected COS-7 and human embryonic kidney 293 cells, all three receptors displayed a high degree of ligand-independent signaling activity. The structurally homologous motilin receptor served as a constitutively silent control; upon agonist stimulation, however, it signaled with a similar efficacy to the three related receptors. The constitutive activity of the ghrelin receptor and of neurotensin receptor 2 through the G(q), phospholipase C pathway was approximately 50% of their maximal capacity as determined through inositol phosphate accumulation. These two receptors also showed very high constitutive activity in activation of cAMP response element-driven transcription. GPR39 displayed a clear but lower degree of constitutive activity through the inositol phosphate and cAMP response element pathways. In contrast, GPR39 signaled with the highest constitutive activity in respect of activation of serum response element-dependent transcription, in part, possibly, through G(12/13) and Rho kinase. Antibody feeding experiments demonstrated that the epitope-tagged ***ghrelin*** receptor was constitutively internalized but could be trapped at the cell surface by an inverse agonist, whereas GPR39 remained at the cell surface. Mutational analysis showed that the constitutive activity of both the ***ghrelin*** receptor and GPR39 could systematically be tuned up and down depending on the size and hydrophobicity of the side chain in position VI:16 in the context of an aromatic residue at VII:09 and a large hydrophobic residue at VII:06. It is concluded that the three ghrelin-like receptors display an unusually high degree of constitutive activity, the structural basis for which is determined by an aromatic cluster on the inner face of the extracellular ends of TMs VI and VII.

CONTROLLED TERM:
Amino Acid Sequence
Animals
COS Cells
Cell Line
Cyclic AMP: ME, metabolism
DNA Mutational Analysis
DNA, Complementary: ME, metabolism
Dose-Response Relationship, Drug
Enzyme-Linked Immunosorbent Assay
GTP-Binding Protein alpha Subunits, G12-G13: ME, metabolism
Humans
Inositol Phosphates: ME, metabolism
Ligands
MAP Kinase Signaling System
Microscopy
Models, Molecular

Molecular Sequence Data
Phosphatidylinositols: CH, chemistry
Phospholipase C: ME, metabolism
Phylogeny
Protein Conformation
Protein Structure, Secondary
Protein Structure, Tertiary
*Receptors, G-Protein-Coupled: CH, chemistry
*Receptors, G-Protein-Coupled: PH, physiology
Receptors, Gastrointestinal Hormone: CH, chemistry
Receptors, Gastrointestinal Hormone: ME, metabolism
Receptors, Neuropeptide: CH, chemistry
Receptors, Neuropeptide: ME, metabolism
*Receptors, Neurotensin: ME, metabolism
Signal Transduction
Transcription, Genetic
Transfection
CAS REGISTRY NO.: 60-92-4 (Cyclic AMP)
CHEMICAL NAME: 0 (DNA, Complementary); 0 (GPR39 protein, human); 0 (Inositol Phosphates); 0 (Ligands); 0 (Phosphatidylinositols); 0 (Receptors, G-Protein-Coupled); 0 (Receptors, Gastrointestinal Hormone); 0 (Receptors, Neuropeptide); 0 (Receptors, Neurotensin); 0 (growth hormone secretagogue receptor); 0 (motilin receptor); EC 3.1.4.3 (Phospholipase C); EC 3.6.1.46 (GTP-Binding Protein alpha Subunits, G12-G13)

L90 ANSWER 6 OF 18 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2004164484 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15058279
TITLE: Constitutive ghrelin receptor activity as a signaling set-point in appetite regulation.
AUTHOR: Holst Birgitte; Schwartz Thue W
CORPORATE SOURCE: Laboratory for Molecular Pharmacology, Department of Pharmacology, The Panum Institute, University of Copenhagen, 7TM Pharma A/S, Denmark.. b.holst@molpharm.dk
SOURCE: Trends in pharmacological sciences, (2004 Mar) Vol. 25, No. 3, pp. 113-7. Ref: 20
Journal code: 7906158. ISSN: 0165-6147.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 3 Apr 2004
Last Updated on STN: 20 Apr 2004
Entered Medline: 19 Apr 2004
CONTROLLED TERM:
Animals
*Appetite: PH, physiology
Eating: PH, physiology
Humans
*Peptide Hormones: PH, physiology
*Receptors, G-Protein-Coupled: PH, physiology
*Signal Transduction: DE, drug effects
CHEMICAL NAME: 0 (Peptide Hormones); 0 (Receptors, G-Protein-Coupled); 0 (ghrelin); 0 (growth hormone secretagogue receptor)

L90 ANSWER 7 OF 18 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2003514700 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12907757
TITLE: High constitutive signaling of the ghrelin receptor--identification of a potent inverse agonist.
AUTHOR: Holst Birgitte; Cygankiewicz Adam; Jensen Tine Halkjaer; Ankersen Michael; Schwartz Thue W
CORPORATE SOURCE: Laboratory for Molecular Pharmacology, Institute of Pharmacology, The Panum Institute, University of Copenhagen, DK-2200 Copenhagen, Denmark.. b.holst@molpharm.dk
SOURCE: Molecular endocrinology (Baltimore, Md.), (2003 Nov) Vol. 17, No. 11, pp. 2201-10. Electronic Publication: 2003-08-07.
Journal code: 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 1 Nov 2003
Last Updated on STN: 14 Jul 2004
Entered Medline: 13 Jul 2004

ABSTRACT:
Ghrelin is a GH-releasing peptide that also has an important role as an orexigenic hormone-stimulating food intake. By measuring inositol phosphate turnover or by using a reporter assay for transcriptional activity controlled by cAMP-responsive elements, the ghrelin receptor showed strong, ligand-independent signaling in transfected COS-7 or human embryonic kidney 293 cells. Ghrelin and a number of the known nonpeptide GH secretagogues acted as agonists stimulating inositol phosphate turnover further. In contrast, the low potency ghrelin antagonist, [D-Arg1,D-Phe5,D-Trp7,9,Leu11]-substance P was surprisingly found to be a high potency (EC50 = 5.2 nm) full inverse agonist as it decreased the constitutive signaling of the ***ghrelin*** receptor down to that observed in untransfected cells. The homologous motilin receptor functioned as a negative control as it did not display any sign of constitutive activity; however, upon agonist stimulation the motilin receptor signaled as strongly as the unstimulated ghrelin receptor. It is concluded that the ghrelin receptor is highly constitutively active and that this activity could be of physiological importance in its role as a regulator of both GH secretion and appetite control. It is suggested that inverse agonists for the ghrelin receptor could be particularly interesting for the treatment of obesity.

CONTROLLED TERM: Amino Acid Sequence
Animals
Cell Line
Cercopithecus aethiops
Cyclic AMP Response Element-Binding Protein: ME, metabolism
Humans
Inositol Phosphates: ME, metabolism
Ligands
Molecular Sequence Data
Molecular Structure
Obesity: ME, metabolism
Peptide Hormones: ME, metabolism
Phospholipase C: ME, metabolism
*Receptors, G-Protein-Coupled: AG, agonists
Receptors, G-Protein-Coupled: AI, antagonists & inhibitors
Receptors, G-Protein-Coupled: CH, chemistry
*Receptors, G-Protein-Coupled: ME, metabolism

Response Elements: GE, genetics
*Signal Transduction
CHEMICAL NAME: 0 (Cyclic AMP Response Element-Binding Protein); 0 (Inositol Phosphates); 0 (Ligands); 0 (Peptide Hormones); 0 (Receptors, G-Protein-Coupled); 0 (ghrelin); 0 (growth hormone secretagogue receptor); EC 3.1.4.3 (Phospholipase C)

L90 ANSWER 8 OF 18 MEDLINE on STN
ACCESSION NUMBER: 2007377132 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17488974
TITLE: GPR39 splice variants versus antisense gene LYPD1: expression and regulation in gastrointestinal tract, endocrine pancreas, liver, and white adipose tissue.
AUTHOR: Egerod Kristoffer L; Holst Birgitte; Petersen Pia S; Hansen Jacob B; Mulder Jan; Hokfelt Tomas; Schwartz Thue W
CORPORATE SOURCE: Laboratory for Molecular Pharmacology, Department of Neuroscience and Pharmacology, University of Copenhagen, DK-2200 Copenhagen, Denmark.
SOURCE: Molecular endocrinology (Baltimore, Md.), (2007 Jul) Vol. 21, No. 7, pp. 1685-98. Electronic Publication: 2007-05-08.
Journal code: 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200708
ENTRY DATE: Entered STN: 28 Jun 2007
Last Updated on STN: 16 Aug 2007
Entered Medline: 15 Aug 2007

ABSTRACT:
G protein-coupled receptor 39 (GPR39) is a constitutively active, orphan member of the ghrelin receptor family that is activated by zinc ions. GPR39 is here described to be expressed in a full-length, biologically active seven-transmembrane form, GPR39-1a, as well as in a truncated splice variant five-transmembrane form, GPR39-1b. The 3' exon of the GPR39 gene overlaps with an antisense gene called LYPD1 (Ly-6/PLAUR domain containing 1). Quantitative RT-PCR analysis demonstrated that GPR39-1a is expressed selectively throughout the gastrointestinal tract, including the liver and pancreas as well as in the kidney and adipose tissue, whereas the truncated GPR39-1b form has a more broad expression pattern, including the central nervous system but with highest expression in the stomach and small intestine. In contrast, the LYPD1 antisense gene is highly expressed throughout the central nervous system as characterized with both quantitative RT-PCR and in situ hybridization analysis. A functional analysis of the GPR39 promoter region identified sites for the hepatocyte nuclear factors 1alpha and 4alpha (HNF-1alpha and -4alpha) and specificity protein 1 (SP1) transcription factors as being important for the expression of GPR39. In vivo experiments in rats demonstrated that GPR39 is up-regulated in adipose tissue during fasting and in response to streptozotocin treatment, although its expression is kept constant in the liver from the same animals. GPR39-1a was expressed in white but not brown adipose tissue and was down-regulated during adipocyte differentiation of fibroblasts. It is concluded that the transcriptional control mechanism, the tissue expression pattern, and in vivo response to physiological stimuli all indicate that the GPR39 receptor very likely is of importance for the function of a number of metabolic organs, including the liver, gastrointestinal tract, pancreas, and adipose tissue.

CONTROLLED TERM: Check Tags: Male
Adipose Tissue: ME, metabolism
Adipose Tissue, Brown: ME, metabolism
Alternative Splicing
Amino Acid Sequence
Animals
*Antisense Elements (Genetics)
Base Sequence
Cell Line
DNA Primers: GE, genetics
Diabetes Mellitus, Experimental: GE, genetics
Diabetes Mellitus, Experimental: ME, metabolism
Gastrointestinal Tract: ME, metabolism
Gene Expression Regulation
Humans
In Situ Hybridization
Islets of Langerhans: ME, metabolism
Liver: ME, metabolism
Models, Molecular
Molecular Sequence Data
Promoter Regions (Genetics)
RNA, Messenger: GE, genetics
RNA, Messenger: ME, metabolism
Rats
Rats, Wistar
Receptors, G-Protein-Coupled: CH, chemistry
*Receptors, G-Protein-Coupled: GE, genetics
*Receptors, G-Protein-Coupled: ME, metabolism
Reverse Transcriptase Polymerase Chain Reaction
Tissue Distribution

CHEMICAL NAME: 0 (Antisense Elements (Genetics)); 0 (DNA Primers); 0 (RNA, Messenger); 0 (Receptors, G-Protein-Coupled)

L90 ANSWER 9 OF 18 MEDLINE on STN
ACCESSION NUMBER: 2006123975 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16511600
TITLE: Ghrelin receptor mutations--too little height and too much hunger.
AUTHOR: Holst Birgitte; Schwartz Thue W
CORPORATE SOURCE: Laboratory for Molecular Pharmacology, Panum Institute, University of Copenhagen, Copenhagen, Denmark.
SOURCE: The Journal of clinical investigation, (2006 Mar) Vol. 116, No. 3, pp. 637-41. Ref: 19
Journal code: 7802877. ISSN: 0021-9738.
COMMENT: Comment on: J Clin Invest. 2006 Mar;116(3):760-8. PubMed ID: 16511605
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200604
ENTRY DATE: Entered STN: 3 Mar 2006
Last Updated on STN: 7 Apr 2006
Entered Medline: 6 Apr 2006

ABSTRACT:
The ghrelin receptor is known from in vitro studies to signal in the absence of the hormone ghrelin at almost 50% of its maximal capacity.

But, as for many other 7-transmembrane receptors, the in vivo importance of this ligand-independent signaling has remained unclear. In this issue of the JCI, Pantel et al. find that a natural mutation in the ghrelin receptor, Ala204Glu, which is associated with a selective loss of constitutive activity without affecting ghrelin affinity, potency, or efficacy, segregates in 2 families with the development of short stature (see the related article beginning on page 760). By combination of the observations from this study with those related to the phenotype of subjects carrying another natural ***ghrelin*** receptor mutation, Phe279Leu, having identical molecular-pharmacological properties, it is proposed that selective lack of ***ghrelin*** receptor constitutive signaling leads to a syndrome characterized not only by short stature, but also by obesity that apparently develops during puberty.

CONTROLLED TERM: *Amino Acid Substitution: GE, genetics
*Body Height: GE, genetics
Humans
*Hunger: PH, physiology
Obesity: GE, genetics
Obesity: ME, metabolism
Obesity: PP, physiopathology
*Peptide Hormones: ME, metabolism
Puberty: GE, genetics
Puberty: ME, metabolism
Receptors, G-Protein-Coupled: DF, deficiency
*Receptors, G-Protein-Coupled: GE, genetics
Receptors, G-Protein-Coupled: PH, physiology
Signal Transduction: GE, genetics
Syndrome

CHEMICAL NAME: 0 (Peptide Hormones); 0 (Receptors, G-Protein-Coupled); 0 (ghrelin); 0 (growth hormone secretagogue receptor)

L90 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2006:410127 CAPLUS Full-text
DOCUMENT NUMBER: 144:445679
TITLE: Uses of growth hormone secretagogues in the treatment of individuals suffering from renal and/or liver failure
INVENTOR(S): Lange, Birgitte Holst; Schambye, Hans T.; Nielsen, Tina Geritz
PATENT ASSIGNEE(S): Gastrotech Pharma A/S, Den.
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006045319	A2	20060504	WO 2005-DK694	20051027
WO 2006045319	A3	20060928		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,

VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

EP 1812044		A2	20070801	EP 2005-796707	20051027

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

PRIORITY APPLN. INFO.:	DK 2004-1654	A	20041027
	DK 2004-1655	A	20041027
	WO 2005-DK694	W	20051027

OTHER SOURCE(S): MARPAT 144:445679

AB The invention relates to the use of a secretagogue compound for the preparation of a medicament for treatment of an individual suffering from renal failure and/or liver failure. Furthermore, the invention relates to a method for stimulating appetite, food intake and/or weight gain in an individual suffering from liver failure and/or renal failure, said method comprising administration of a secretagogue to said patient.

CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 15

IT 304853-26-7, Ghrelin 304853-26-7D, Growth hormone secretagogue, -like compds. and salts
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(uses of growth hormone secretagogues in treatment of individuals suffering from renal and/or liver failure)

L90 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4

ACCESSION NUMBER:	2006:412018 CAPLUS Full-text
DOCUMENT NUMBER:	144:404881
TITLE:	Use of a growth hormone secretagogue for increasing or maintaining lean body mass and/or for treatment of chronic obstructive pulmonary disease
INVENTOR(S):	Lange, Birgitte Holst; Schambye, Hans T.; Nielsen, Tina Geritz
PATENT ASSIGNEE(S):	Gastrotech Pharma A/S, Den.
SOURCE:	PCT Int. Appl., 78 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006045314	A2	20060504	WO 2005-DK689	20051026
WO 2006045314	A3	20070412		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.:	DK 2004-1657	A	20041027
	DK 2005-242	A	20050216
	US 2005-653116P	P	20050216

OTHER SOURCE(S): MARPAT 144:404881

AB The present invention relates to a method for increasing or maintaining lean body mass in an individual in need thereof, by administering a secretagogue. The present invention also relates in another aspect to the use of a secretagogue for the production of a medicament for use in increasing or maintaining an individual's lean body mass, preferably in an individual suffering from, or at risk of suffering from, cachexia, such as cancer cachexia.

IC ICM A61K

CC 2-5 (Mammalian Hormones)

IT 258279-04-8, Human ghrelin 304853-26-7, Ghrelin 304853-26-7D, Ghrelin, salts and -like compds.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of a growth hormone secretagogue for increasing or maintaining lean body mass and/or for treatment of chronic obstructive pulmonary disease)

L90 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 6

ACCESSION NUMBER:	2005:1130666 CAPLUS Full-text
DOCUMENT NUMBER:	143:385176
TITLE:	Prolonging the biological activity of human ghrelin secretagogue
INVENTOR(S):	Hansen, Christian
PATENT ASSIGNEE(S):	Gastrotech Pharma A/S, Den.
SOURCE:	PCT Int. Appl., 88 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005097831	A2	20051020	WO 2005-DK241	20050407
WO 2005097831	A3	20051222		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	DK 2004-574	A	20040407

AB The author discloses the use of immunol. and non-immunol. biomols. that target human ghrelin or ghrelin-like compds. In one aspect, these biomols. comprise antibodies and/or affibodies for mediating appetite regulation in an individual by prolonging the serum half-life of ghrelin.

IC ICM C07K016-18
ICS A61K039-395

CC 15-3 (Immunochemistry)

Section cross-reference(s): 1, 14, 63
IT 304853-26-7D, Ghrelin, derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced serum half-life of)

L90 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 2005:1123798 CAPLUS Full-text
DOCUMENT NUMBER: 143:400386
TITLE: Use of a secretagogue for the treatment of ghrelin deficiency
INVENTOR(S): Nilsson, Henrik; Lange, Birgitte Holst; Post, Claes; Nielsen, Tina Geritz
PATENT ASSIGNEE(S): Gastrotech Pharma A/S, Den.
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005097173	A2	20051020	WO 2005-DK237	20050407
WO 2005097173	A3	20051229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1742655	A2	20070117	EP 2005-715155	20050407
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				

PRIORITY APPLN. INFO.:
DK 2004-569 A 20040407
DK 2004-1656 A 20041027
WO 2005-DK237 W 20050407

OTHER SOURCE(S): MARPAT 143:400386

AB The present invention relates to the use of a growth hormone (GH) secretagogue, such as a ghrelin-like compound, for the preparation of a medicament for the prophylaxis or treatment of ghrelin deficiency, and/or undesirable symptoms associated therewith, in an individual at risk of acquiring partial or complete ghrelin deficiency resulting from a medical treatment and/or from a pathol. condition. The present invention also relates to use of a secretagogue compound for the preparation of a medicament for the prophylaxis or treatment of one or more of: loss of fat mass, loss of lean body mass, weight loss, cachexia, loss of appetite, immunol. dysfunction, malnutrition, disrupted sleep pattern, sleepiness, reduction in intestinal absorption and/or intestinal mobility problems in an individual suffering from, or at risk of suffering from, ghrelin deficiency. Furthermore, the present invention relates to the use of a secretagogue, such as a ghrelin-like compound, for the production of a medicament for preventing weight increase in an individual either: (a) being converted from a hyperthyroidic state to

euthyroid state, or (b) in remission from being converted from a hyperthyroidic state to euthyroid state.
IC ICM A61K038-25
ICS A61P003-00; A61P005-14
CC 2-6 (Mammalian Hormones)
IT 304853-26-7D, Ghrelin, -like compds.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of a secretagogue for treatment of symptoms associated with ghrelin deficiency caused by pathol. conditions)

L90 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 2005:136591 CAPLUS Full-text
DOCUMENT NUMBER: 142:233847
TITLE: Uses of ghrelin-like secretagogues for treatment of cancer cachexia
INVENTOR(S): Lange, Birgitte Holst; Hansen, Christian; Nilsson, Henrik
PATENT ASSIGNEE(S): Gastrotech Pharma A/S, Den.
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014032	A2	20050217	WO 2004-DK529	20040806
WO 2005014032	A3	20050317		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1660117	A2	20060531	EP 2004-739026	20040806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1863550	A	20061115	CN 2004-80029235	20040806
JP 2007523048	T	20070816	JP 2006-522237	20040806
IN 2006CN00784	A	20070622	IN 2006-CN784	20060303
US 2007037751	A1	20070215	US 2006-567406	20061019 <--

PRIORITY APPLN. INFO.:
DK 2003-1139 A 20030806
DK 2003-1140 A 20030806
US 2003-494815P P 20030814
US 2003-494816P P 20030814
DK 2003-1283 A 20030905
DK 2003-1569 A 20031024
DK 2003-1570 A 20031024
DK 2004-570 A 20040407
WO 2004-DK529 W 20040806

OTHER SOURCE(S): MARPAT 142:233847

AB The present invention relates, in one aspect, to the use of a secretagogue compound for the preparation of a medicament for the prophylaxis or treatment

of cancer cachexia in an individual in need of such treatment. In another aspect, the present invention relates to the use of a ghrelin-like compound for the preparation of a medicament for prophylaxis or treatment of cachexia in an individual by administering a s.c. dosage of said medicament to the individual. In a further aspect, the present invention relates to the use of a ghrelin-like compound or a pharmaceutically acceptable salt thereof for the preparation of a medicament for stimulation of appetite in an individual by administering a s.c. dosage of said medicament to the individual. Furthermore, the present invention relates to a number of new ghrelin-like compds. and uses thereof, as well as to pharmaceutical compns. and medical packaging comprising the new ghrelin-like compds.

IC ICM A61K038-25
ICS C07K014-60; G01N033-74; A61P001-14

CC 2-6 (Mammalian Hormones)
Section cross-reference(s): 34

IT 258279-04-8P 304853-26-7DP, Ghrelin, -like compds. 321974-68-9P 843660-25-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(uses of ghrelin-like secretagogues for treatment of cancer cachexia)

L90 ANSWER 15 OF 18 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2007-008841 [01] WPIX
DOC. NO. CPI: C2007-003140 [01]
TITLE: Novel growth hormone secretagogue receptor 1A ligand compound useful for treating growth hormone secretagogue receptor 1A associated diseases such as cachexia
DERWENT CLASS: B04; B05; D13; D16
INVENTOR: JENSEN P H; LANGE B H; SCHAMBYE H T
PATENT ASSIGNEE: (GAST-N) GASTROTECH PHARMA AS
COUNTRY COUNT: 111

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2006058539	A2	20060608	(200701)*	EN	138[3]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2006058539	A2	WO 2005-DK763	20051129

PRIORITY APPLN. INFO: DK 2004-1875 20041130
INT. PATENT CLASSIF.:
IPC ORIGINAL: A61K [,S]
BASIC ABSTRACT:
WO 2006058539 A2 UPAB: 20070102
NOVELTY - Growth hormone secretagogue receptor 1A (GHS-R1A) ligand compounds (I'), (I), (I'') and (I'''), are new.
DETAILED DESCRIPTION - Growth hormone secretagogue receptor 1A (GHS-R1A) ligand compound is chosen from compound of formula (II): Z2-(X3)n-(X2)-(X1)m-Z3-Z1, compound of formula (I): Z1-(X1)m-(X2)-(X3)n- Z2, compound of formula (III): Z1-X1-X2-X3-X4-X5-X6-Z2, and compound of formula (IV): Z1-R1-(X2)-(X3)n-Z2, or its salt. In formula (II):

Z1,Z2=optionally present protecting group; X1=amino acid; X2=anchor group, preferably amino acid being modified; X3=amino acids, in which at least one (X3) is a D-amino acid; Z3=optionally present linker or C-terminal group; m=0-3; and
n=0-35, in which both n and m cannot be 0. In formula (I):
Z1,Z2,X1=same as defined above; X2=anchor group chosen from amino acid being modified with glycerophospholipid, sterol moiety, sphingolipid moiety, ceramide or its analog, isoprenoid pyrophosphate, glycosyl-phosphatidylinositol (GPI) anchor, or phosphatidyl serine or its analog, or alternatively X2 is chosen from L or D form of decenoic acid, Trp(5-NH2), 5-hexenoic acid, 6-heptenoic acid, 7-octenoic acid, 8-nonenoic acid, Ala-3-cp, Ala-3-cb, Phe-4-Me, Phe-4-Et, Phe-4-iPr, Phe-4-Ph, beta-MeTrp, Ala(3-(3-Quinolinyl)), Ala(3-(2-benzimidazoyl)), BenzoTrp and 7-AzaTrp; X3=amino acid; m=0-10; and
n=0-35, in which m and n cannot both be 0. In formula (III):
Z1,Z2=same as defined above; X1=amino acid having a structure of formula (B); X7=spacer with length of 1-8 chemical bonds; X8=hydrogen bond donor such as amine or hydroxyl group; X2,X3,X5=aromatic amino acids; X4=optionally present amino acid; and X6=optionally present and chosen from alcohol, ether, hydrocarbon, hydrazine, peptide and peptidomimetic moiety. Where at least one of X1-X5 is a D-amino acid. In formula (IV): R1=betaAla-, betaAla-X1-, GABA-, GABA-X1-, aminopentanoyl-X1, hydroxy acetic acid (HAA)-, HAA-X1-, or compound of formula (B); X7,X8=same as defined above; Z1,Z2,X1=same as defined above; X2=anchor group such as any amino acid being modified with a bulky group; X3=amino acid, or optionally an anchor group; and n=0-35.
INDEPENDENT CLAIMS are also included for: (1) pharmaceutical composition comprising the GHS-R1A ligand compound or its salt, and carrier, vehicles and/or excipients; (2) a medical packaging comprising one or more dosage units of the pharmaceutical composition; and
(3) treatment comprising administering GHS-R1A ligand compound or its salt to an individual in need of treatment. ACTIVITY - Antidiabetic; Cardiant; Antiinflammatory; Cytostatic; Immunomodulator; Osteopathic; Endocrine-Gen.; Antithyroid; Anorectic; Eating-Disorders-Gen.
Sprauge-Dawley rats were used in the study. The animals were caged individually and fed with a commercial diet. All animals were allowed on acclimatization period of minimum of 7 days prior to the commencement of the experiment. The animals were separated in six groups and each group was respectively treated twice daily with subcutaneous injection of sodium chloride solution (control), 200 micrograms/kg body weight of ghrelin (positive control), 50 or 200 micrograms/kg body weight of GTP-5 and GTP-6 (growth hormone secretagogue receptor 1A (GHS-R1A) ligand compound). The weight of the animals, and their food and water were recorded daily. The animals were killed and epididymal, subcutaneous and retroperitoneal fat pads were dissected and weighed. The ghrelin group gained significantly more weight than the saline group. Furthermore, the GTP-5 and GTP-6 groups showed higher weight gain and cumulative food intake than saline group. Ghrelin, GTP-5 and GTP-6 were found to induce an increase in subcutaneous fat depots.
MECHANISM OF ACTION - Modulator of GHS-R1A.
USE - The GHS-R1A ligand compound or its salt, is useful for the preparation of medicament for the treatment of an individual (claimed). The GHS-R1A ligand compound is useful for treating and/or preventing GHS-R1A associated diseases such as cachexia in individuals suffering from disease (e.g. cancer, AIDS, cardiac failure, liver failure and chronic infection), heart failure, bone and cartilage related disease, bone fracture, inflammatory diseases, malignant disease, hyperthyroidism, obesity and diabetes, and in preparation of medicament for stimulation of appetite, food intake and/or weight gain, and for increasing body fat mass and/or lean body mass.
ADVANTAGE - The anchor groups improve the anchorage of the GHS-R1A ligand in the cell membrane and thus improve the efficacy of GHS-R1A ligand. The GHS-R1A exhibits increase half-life in blood. DESCRIPTION OF DRAWINGS - The figure shows a

graph representing the total weight gain of rats treated with the growth hormone secretagogue receptor 1A ligand compound, saline or ghrelin. MANUAL CODE:
CPI: B04-B01B; B04-C01H; B04-N04A; B04-N04A0E; B11-C06;
B14-C03; B14-E11B; B14-E12; B14-F01B; B14-H01;
B14-L01; B14-L06; B14-N01; B14-N11; B14-S04; D03-H01T2;
D05-H17A

TECH

BIOTECHNOLOGY - Preparation (disclosed): The GHS-R1A ligand compound is prepared by standard peptide synthesis and recombinant methods.
Preferred Compound: The GHS-R1A ligand compound of formula (II) is chosen from compound of formula (IIa): Z2-(X3)n-(X2)-(X1)m-1-Gly-Z1, formula (IIIa): Z2-(X3)n-(X2)-D-Ser-Gly-Z1, formula (IVa): Z2-(X3)n-(X2)-Gly-Z1, and formula (Va): Z2-(X3)n-D-Ser-Z3-Z1, preferably compound of formula (IIIa). The GHS-R1A ligand compound of formula (II) comprises a structure of formula (VIa').
R1=alcohol, ether, hydrocarbon, hydrazine, peptide or peptidomimetic moiety;
R2=aromatic moiety;
R3,R5=H or CH3;
R4=aromatic, hydrophobic or amphiphilic moiety;
R6=spacer with length of 1-8 chemical bonds;and
R7=hydrogen bond donor such as NH2 or OH.
The GHS-R1A ligand compound of formula (I) is chosen from a compound of formula (IIb): Z1-Gly-(X1)m-1-(X2)-(X3)n-Z2, formula (IIIb): Z1-Gly-Ser-(X2)-(X3)n-Z2, and formula (IVb): Z1-Gly-(X2)-(X3)n-Z2, preferably compound of formula (IIIb). The GHS-R1A ligand compound of formula (IV) is chosen from compound of formula (IId): Z1-betaAla-(X2)-(X3)n-Z2, compound of formula (IIId): Z1-betaAla-Ser-(X2)-(X3)n-Z2, compound of formula (IVd): Z1-GABA-(X2)- (X3)n-Z2, compound of formula (Vd): Z1- GABA-Ser-(X2)-(X3)n-Z2, compound of formula (VIId): Z1-aminopentanoyl-Ser-(X2)-(X3)n- Z2, compound of formula (VIIId): Z1-HAA-Ser-(X2)-(X3)n-Z2, and compound of formula (IXd): Z1-HAA-(X2)-(X3)n- Z2, in which Z1 and Z2 are optional protecting groups.
Preferred Composition: The composition further comprises transport molecules such as liposomes, micelles, iscoms and/or microspheres.
Preferred Medicament: The medicament comprises the GHS-R1A ligand compound or its salt as a lyophilisate, and the medicament further comprises a solvent, where the lyophilisate and the solvent are in separate compartments until administration. The medicament comprises a solution of the GHS-R1A ligand compound or its salt. The solvent is saline.

L90 ANSWER 16 OF 18 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-317315 [33] WPIX
DOC. NO. CPI: C2006-104292 [33]
TITLE: Use of secretagogue compound in the preparation of medicament for stimulation of appetite, food intake and/or weight gain in transplantation patient
DERWENT CLASS: B04
INVENTOR: LANGE B H; NIELSEN T G; SCHAMBYE H T; LANGE B; NIELSEN T; SCHAMBYE H
PATENT ASSIGNEE: (GAST-N) GASTROTECH PHARMA AS
COUNTRY COUNT: 111

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2006045313	A2	20060504	(200633)*	EN	74[0]	
EP 1812045	A2	20070801	(200753)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2006045313 A2		WO 2005-DK688	20051026
EP 1812045 A2		EP 2005-796749	20051026
EP 1812045 A2		WO 2005-DK688	20051026

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1812045	A2	Based on	WO 2006045313	A

PRIORITY APPLN. INFO: DK 2004-1658 20041027
INT. PATENT CLASSIF.:
IPC ORIGINAL: A61K0038-22 [I,A]; A61K0038-22 [I,C]; A61P0001-00 [I,C]; A61P0001-14 [I,A]; A61K0038-22 [I,C]; A61P0001-00 [I,C]

BASIC ABSTRACT:

WO 2006045313 A2 UPAB: 20060523
NOVELTY - Use of a secretagogue compound in the preparation of a medicament for the stimulation of appetite, food intake and/or weight gain in a transplantation patient, is new. ACTIVITY - Anabolic.
MECHANISM OF ACTION - None given.
USE - For the stimulation of appetite, food intake and/or weight gain in a transplantation (preferably lung, kidney, liver or heart transplantation) patient having a lean body mass of less than 80% (preferably less than 60%) of normal and/or a body mass index below 17 kg/m2 (claimed).
ADVANTAGE - The orexigenic and metabolic effects of secretagogues, such as ghrelin, reduce the morbidity and mortality in patients undergoing organ transplantation; and improve their quality of life. The medicament increases body fat mass and/or lean body mass. MANUAL CODE: CPI: B04-J01; B14-E11

TECH

PHARMACEUTICALS - Preferred Compound: The secretagogue is ghrelin or its salt; or a ghrelin-like compound comprising a structure of formula Z1-(X1)m-(X2)-(X3)n-Z2 (I) or its salt (preferably of formula Z1-Gly-Ser-(X2)-(X3)n-Z2 (III)).
Z1 and Z2 = an optionally present protecting group;
X1 = a naturally occurring and synthetic amino acid;
X2 = a naturally occurring and synthetic amino acid that is modified with a bulky hydrophobic group (preferably acyl (preferably 1-35C acyl, especially 8-11C acyl) or a fatty acid) (preferably modified Ser, Cys or Lys, especially modified Ser);
X3 = a naturally occurring and synthetic amino acid (preferably 25 amino acid sequences as given in the specification e.g. Phe-Leu-Ser-Pro-Glu-His-Gln or Phe-Leu-Ser-Pro-Glu-His-Gln-Arg-Val-Gln-Gln-Arg-Lys-Glu-Ser-Lys-Lys-Pro-Pro-Ala);
m = 1 - 10 (preferably 1 - 9, especially 2);
n = 0 - 35 (preferably 1 - 25, especially 1 - 10 or 15 - 24).
At least one of X1 and X3 may be modified with a bulky hydrophobic group (preferably an acyl or a fatty acid).
Preferred Medicament: The medicament is in the form of a formulation that comprises the secretagogue or its salt as a lyophilizate, and a solvent (preferably saline) in separate compartments until administration. The medicament is given until the lean body mass is more than 60% (preferably more than 80%, especially more than 90%) of normal.
Preferred Transplant: The transplant is a solid organ (preferably lung, heart, liver, kidney, pancreas, intestine or an extremity); hematopoietic stem cell transplantation (preferably bone marrow transplantation or peripheral blood stem cell transplantation); or a reconstructive plastic

surgery, such as reconstructive facial surgery, or reconstructive surgery after burns.

L90 ANSWER 17 OF 18 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-703468 [72] WPIX
DOC. NO. CPI: C2005-214152 [72]
TITLE: Use of a secretagogue in combination with a growth hormone for the preparation of a medicament to treat or prevent e.g. cardiac cachexia, cancer cachexia and acquired immunodeficiency syndrome wasting
DERWENT CLASS: B04; B07
INVENTOR: ISAKSSON O G P; LANGE B H; NIELSEN T G; POST C
PATENT ASSIGNEE: (GAST-N) GASTROTECH PHARMA AS
COUNTRY COUNT: 108

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005097174	A2	20051020	(200572)*	EN	89[0]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005097174	A2	WO 2005-DK242	20050407

PRIORITY APPLN. INFO: DK 2004-575 20040407
INT. PATENT CLASSIF.:
IPC RECLASSIF.: A61K0038-24 [I,A]; A61K0038-24 [I,C]; A61K0038-25 [I,A]; A61K0038-25 [I,C]; A61K0038-27 [I,A]; A61K0038-27 [I,C]; A61K0038-33 [I,C]; A61K0038-35 [I,A]

BASIC ABSTRACT:
WO 2005097174 A2 UPAB: 20051223
NOVELTY - Use of a secretagogue (A) or its salts in combination with a growth hormone (B) or its salts for the preparation of a medicament.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a composition comprising (A) and (B) and/or their salts and carriers, vehicles and/or excipients; (2) a medical packaging comprising one or more dosage units of the composition; and
(3) a method for monitoring the effect of a treatment of an individual with a secretagogue compound in combination with (B), comprising measuring the blood level in the individual of insulin like growth factor (IGF)-1, IGFBP-3 and/or ALS. ACTIVITY - Immunomodulator; Anti-HIV; Cardiant; Cytostatic; Antilipemic; Endocrine-Gen.; Anabolic.
MECHANISM OF ACTION - Growth hormone secretagogue receptor 1a (GHS-R1a) ligand modulator. (A) Was tested for its GHS-R1a ligand modulatory activity using biological assay. The results showed that the median effective concentration of (A) was less than 0.01 nM.
USE - (A) In combination with (B) is useful for the preparation of a medicament to treat or prevent pathological conditions or the condition or frailty, where the condition is cachexia (where the cachexia is associated with human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS) such as AIDS wasting) (cardiac cachexia, cancer cachexia (where the cancer is lung cancer, pancreatic cancer, liver cancer and a gastrointestinal tract cancers)) and lipodystrophy, stimulate appetite, food intake and weight gain, increase body fat mass and/or maintain lean body mass, treat dwarfism and/or growth retardation, that are caused by the individual having insufficient physiological levels of growth hormone (claimed).

ADVANTAGE - The combination of (A) and (B) has synergistic effect. MANUAL CODE: CPI: B04-B04D5; B04-C01G; B04-H01; B04-H06H; B04-J01; B04-J05; B04-N0200E; B11-C06; B11-C08E; B12-K04A; B12-M11E; B12-M11F; B14-E11B; B14-F01; B14-F06A; B14-G01B; B14-H01; B14-S02

TECH
PHARMACEUTICALS - Preferred Method: Treatment of cancer comprises administration of (A) in combination with (B) and an anti-neoplastic treatment (a chemotherapy medicament and/or radiotherapy). Treatment of AIDS wasting, cardiac cachexia or the condition or frailty comprises administration of the composition in combination with a NSAID medicament.
Preferred Components: (B) Comprises a fully.defined 748 amino acid (SEQ ID No: 4-8) sequence given in the specification. (B) Is a mammalian growth hormone, growth hormone of a domestic animal (preferably somatotropin or its any isoforms, thyroid stimulating hormone, adrenocorticotropic hormone, leutinizing hormone and/or follicle stimulating hormone) or their homologs, variants or functional equivalents. (B) Comprises a recombinant polypeptide. (B) Is monomeric human growth hormone (hGH), dimeric hGH, trimeric hGH, tetrameric hGH, pentameric hGH, non-covalent oligomers of hGH, disulfide oligomers of hGH, covalently linked hGH, 22K-GHBP complex, 22K-alpha2-macroglobulin complex, 20K-GHBP complex, 20K-alpha2-macroglobulin complex, hGH-V_GHBP complex, hGH-22K, hGH-20K N-alpha-acetylated hGH-22K, Asn152-desamido-hGH-22K, Gln-137-desamido-hGH-22K, hGH-V or placental GH or Glyco-hGH-Vorglycosylated placental growth hormone. (A) Is ghrelin (human ghrelin), a ghrelin-like compound or their salts. The ghrelin-like compound comprises formulae of (Z1-(X1)m-(X2)-(X3)n-Z2 (I), Z1-Gly-(X1)m-1-(X2)-(X3)n-Z2 (II), Z1-Gly-Ser-(X2)-(X3)n-Z2 (III) (preferred) or Z1-Gly-(X2)-(X3)n-Z2 (IV)).
Z1 = an optionally present protecting group;
X1, X3 = an amino acid (naturally occurring and synthetic amino acids) (where the amino acid is modified with a bulky hydrophobic group, preferably an acyl group or a fatty acid) (preferably (X3)n comprises a sequence of (where (X3)n comprises a sequence of Phe-Leu-Ser-Pro-Glu-His-Gln, Phe-Leu-Ser-Pro-Glu-His, Phe-Leu-Ser-Pro-Glu, Phe-Leu-Ser-Pro, Phe-Leu-Ser, Phe-Leu or Phe);
X2 = any amino acid from naturally occurring and synthetic amino acid (where the amino acid being modified with a bulky hydrophobic group (preferably an acyl group or a fatty acid) (preferably modified Ser, modified Cys or modified Lys);
Z2 = an optionally present protecting group;
m = 1-10 (preferably 2); and
n = 0 or 1-35 (preferably 15-24).
Where the acyl group is preferably 1-35C.
Preferred Composition: The medicament is in a formulation for subcutaneous, parenteral, nasal or pulmonary administration. The combination of (A) and (B) formulation is a lyophilizate, and the formulation further comprises a solvent (saline), where the lyophilizate and the solvent are in separate compartments until administration. The composition further comprises transport molecules, such as liposomes, micelles, iscoms and/or microspheres. The medical packaging comprises 1-3 (preferably 3) dosage units or 7-21 (preferably 7, 14 or 21) dosage units. The medical packaging comprises instructions for administering the composition. The instructions includes instructions referring to administration of the composition during a meal or at the most 90 minutes prior to a meal, such as at the most 45 minutes prior to a meal, preferably immediately prior to a meal. The packaging is in the form of a cartridge, such as a cartridge for an injection pen.

L90 ANSWER 18 OF 18 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006106751 EMBASE Full-text
TITLE: Ghrelin receptor mutations - Too little height and too much hunger.
AUTHOR: Holst B.; Schwartz T.W.
CORPORATE SOURCE: T.W. Schwartz, Laboratory for Molecular Pharmacology, Panum Institute, University of Copenhagen, Blegdamsvej 3, Copenhagen, Denmark. schwartz@molpharm.dk
SOURCE: Journal of Clinical Investigation, (1 Mar 2006) Vol. 116, No. 3, pp. 637-641.
Refs: 19
ISSN: 0021-9738 E-ISSN: 1558-8238 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 22 Mar 2006
Last Updated on STN: 22 Mar 2006

ABSTRACT: The ghrelin receptor is known from in vitro studies to signal in the absence of the hormone ghrelin at almost 50% of its maximal capacity. But, as for many other 7-transmembrane receptors, the in vivo importance of this ligand-independent signaling has remained unclear. In this issue of the JCI, Pantel et al. find that a natural mutation in the ghrelin receptor, Ala-204Glu, which is associated with a selective loss of constitutive activity without affecting ghrelin affinity, potency, or efficacy, segregates in 2 families with the development of short stature (see the related article beginning on page 760). By combination of the observations from this study with those related to the phenotype of subjects carrying another natural ghrelin receptor mutation, Phe279Leu, having identical molecular-pharmacological properties, it is proposed that selective lack of ghrelin receptor constitutive signaling leads to a syndrome characterized not only by short stature, but also by obesity that apparently develops during puberty.

CONTROLLED TERM: Medical Descriptors:
*short stature: ET, etiology
*obesity: ET, etiology
hormone action
hormone binding
phenotype
puberty
food intake
cross fertilization
genetic analysis
structure activity relation
physiology
energy expenditure
developmental disorder: ET, etiology
body growth
gene mutation
amino acid substitution
hormone release
heterozygosity
ligand binding

human
review
priority journal
CONTROLLED TERM: Drug Descriptors:
*hormone receptor: EC, endogenous compound
*ghrelin receptor: EC, endogenous compound
ghrelin: EC, endogenous compound
G protein coupled receptor: EC, endogenous compound
appetite stimulant: EC, endogenous compound
unclassified drug
CAS REGISTRY NO.: (ghrelin) 258279-04-8, 304853-26-7

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TEXT SEARCH

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L7             1 SEA FILE=REGISTRY ABB=ON  304853-26-7
L8            75 SEA FILE=CAPLUS ABB=ON  L7/D
L9          3047 SEA FILE=CAPLUS ABB=ON  CACHEXIA/OBI
L10         1571 SEA FILE=CAPLUS ABB=ON  WASTING/OBI
L11        20291 SEA FILE=CAPLUS ABB=ON  APPETITE/OBI
L12         5750 SEA FILE=CAPLUS ABB=ON  MALNUTRITION/OBI
L14       497406 SEA FILE=CAPLUS ABB=ON  NEOPLAS?/OBI
L17           29 SEA FILE=CAPLUS ABB=ON  L8(L)(THU OR PAC OR PKT OR DMA)/RL
L19        27682 SEA FILE=CAPLUS ABB=ON  BODY WEIGHT/CT
L20           35 SEA FILE=CAPLUS ABB=ON  L8 AND ((L9 OR L10 OR L11 OR L12 OR
                 L19) OR (L17 AND L14))


=> s 120 not 122

L95           30 L20 NOT L22

=> fil medl; d que 142; d que 149; d que 151; d que 154; d que 159

FILE 'MEDLINE' ENTERED AT 14:52:07 ON 20 SEP 2007

 FILE LAST UPDATED: 19 Sep 2007 (20070919/UP).  FILE COVERS 1950 TO DATE.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


L28         2304 SEA FILE=MEDLINE ABB=ON  GHRELIN
L30         2202 SEA FILE=MEDLINE ABB=ON  PEPTIDE HORMONES/CT
L32         2754 SEA FILE=MEDLINE ABB=ON  CACHEXIA/CT
L39          526 SEA FILE=MEDLINE ABB=ON  L30(L)(AD OR PD OR TU OR PK)/CT
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L42           13 SEA FILE=MEDLINE ABB=ON  L39 AND L32 AND L28



L28         2304 SEA FILE=MEDLINE ABB=ON  GHRELIN
L30         2202 SEA FILE=MEDLINE ABB=ON  PEPTIDE HORMONES/CT
L33          553 SEA FILE=MEDLINE ABB=ON  WASTING SYNDROME/CT
L49            1 SEA FILE=MEDLINE ABB=ON  L28 AND L30 AND L33



L28         2304 SEA FILE=MEDLINE ABB=ON  GHRELIN
L30         2202 SEA FILE=MEDLINE ABB=ON  PEPTIDE HORMONES/CT
L35         8287 SEA FILE=MEDLINE ABB=ON  EATING/CT(L)DE/CT
L36         4131 SEA FILE=MEDLINE ABB=ON  APPETITE/CT
L39          526 SEA FILE=MEDLINE ABB=ON  L30(L)(AD OR PD OR TU OR PK)/CT
L44          351 SEA FILE=MEDLINE ABB=ON  L39/MAJ
L45          318 SEA FILE=MEDLINE ABB=ON  L44 AND L28
L50       748646 SEA FILE=MEDLINE ABB=ON  NEOPLASMS+NT/CT(L)TH./CT
L51            1 SEA FILE=MEDLINE ABB=ON  (L35 OR L36) AND L45 AND L50



L28         2304 SEA FILE=MEDLINE ABB=ON  GHRELIN
L32         2754 SEA FILE=MEDLINE ABB=ON  CACHEXIA/CT
L33          553 SEA FILE=MEDLINE ABB=ON  WASTING SYNDROME/CT
L35         8287 SEA FILE=MEDLINE ABB=ON  EATING/CT(L)DE/CT
L36         4131 SEA FILE=MEDLINE ABB=ON  APPETITE/CT
L53           19 SEA FILE=MEDLINE ABB=ON  L28(W)LIKE
L54            1 SEA FILE=MEDLINE ABB=ON  L53 AND (L32 OR L33 OR L35 OR L36)



L28         2304 SEA FILE=MEDLINE ABB=ON  GHRELIN
L30         2202 SEA FILE=MEDLINE ABB=ON  PEPTIDE HORMONES/CT
L32         2754 SEA FILE=MEDLINE ABB=ON  CACHEXIA/CT
L33          553 SEA FILE=MEDLINE ABB=ON  WASTING SYNDROME/CT
L35         8287 SEA FILE=MEDLINE ABB=ON  EATING/CT(L)DE/CT
L36         4131 SEA FILE=MEDLINE ABB=ON  APPETITE/CT
L52       725074 SEA FILE=MEDLINE ABB=ON  ANALOG? OR SECRETAGOG? OR DERIVATI?
L59            6 SEA FILE=MEDLINE ABB=ON  L28(1A)L52 AND L30 AND (L32 OR L33 OR
                 L35 OR L36)


=> s 142,149,151,154,159 not 143

L96           21 (L42 OR L49 OR L51 OR L54 OR L59) NOT L43

=> fil embase; d que 161; d que 170; d que 173

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 FILE COVERS 1974 TO 20 Sep 2007 (20070920/ED)

 EMBASE is now updated daily.  SDI frequency remains weekly (default)
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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
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L61           7 SEA FILE=EMBASE ABB=ON  GHRELIN DERIVATIVE/CT



L60        2434 SEA FILE=EMBASE ABB=ON  GHRELIN/CT
L66          14 SEA FILE=EMBASE ABB=ON  CANCER CACHEXIA/CT OR CANCER CACHEXIA
               SYNDROME/CT
L70           3 SEA FILE=EMBASE ABB=ON  L66 AND L60



L60        2434 SEA FILE=EMBASE ABB=ON  GHRELIN/CT
L67        3660 SEA FILE=EMBASE ABB=ON  CACHEXIA/CT
L69         459 SEA FILE=EMBASE ABB=ON  L60(L)(AD OR DT OR PK OR DO OR PD)/CT
L71         721 SEA FILE=EMBASE ABB=ON  L67(L)(DT OR PC)/CT
L73           8 SEA FILE=EMBASE ABB=ON  L69/MAJ AND L71/MAJ


=> s l61,l70,l73 not l65

L97          17 (L61 OR L70 OR L73) NOT L65

=> fil wpix; d que l85

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FILE LAST UPDATED:                    14 SEP 2007   <20070914/UP>
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http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<
'BI ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE


L79        3107 SEA FILE=WPIX ABB=ON  CACHEXIA/BI,ABEX OR CACHECTIC?/BI,ABEX
L80         570 SEA FILE=WPIX ABB=ON  B14-E11B/MC OR C14-E11B/MC
L81         212 SEA FILE=WPIX ABB=ON  GHRELIN/BI,ABEX
L82      542701 SEA FILE=WPIX ABB=ON  ANALOG?/BI,ABEX OR SECRETAGOG?/BI,ABEX
               OR DERIVATI?/BI,ABEX
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L84          23 SEA FILE=WPIX ABB=ON  L81(1A)L82
L85          10 SEA FILE=WPIX ABB=ON  L84 AND (L79 OR L80)


=> s l85 not l88

L98           7 L85 NOT L88

=> => dup rem l96,l95,l98,l97
FILE 'MEDLINE' ENTERED AT 14:52:46 ON 20 SEP 2007

FILE 'CAPLUS' ENTERED AT 14:52:46 ON 20 SEP 2007
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PROCESSING COMPLETED FOR L96
PROCESSING COMPLETED FOR L95
PROCESSING COMPLETED FOR L98
PROCESSING COMPLETED FOR L97
L99          66 DUP REM L96 L95 L98 L97 (9 DUPLICATES REMOVED)
                ANSWERS '1-21' FROM FILE MEDLINE
                ANSWERS '22-51' FROM FILE CAPLUS
                ANSWERS '52-55' FROM FILE WPIX
                ANSWERS '56-66' FROM FILE EMBASE

=> d iall 1-21; d ibib ab hitind 22-51; d iall abeq tech 52-55; d iall 56-66; fil
hom

L99  ANSWER 1 OF 66     MEDLINE on STN                  DUPLICATE 1
ACCESSION NUMBER:   2007294994     MEDLINE  Full-text
DOCUMENT NUMBER:    PubMed ID: 17347304
TITLE:              Ghrelin treatment causes increased food intake
                    and retention of lean body mass in a rat model of cancer
                    cachexia.
AUTHOR:             DeBoer Mark D; Zhu Xin Xia; Levasseur Peter; Meguid Michael
                    M; Suzuki Susumu; Inui Akio; Taylor John E; Halem Heather
                    A; Dong Jesse Z; Datta Rakesh; Culler Michael D; Marks
                    Daniel L
CORPORATE SOURCE:   Center for the Study of Weight Regulation, Oregon Health
                    and Science University, 707 SW Gaines Road, Portland, OR
                    97239, USA.
CONTRACT NUMBER:    1K08 DK 062207-01 (NIDDK)
                    DK/NCI 43796/70239
                    F32 DK 072820-01A1 (NIDDK)
                    R01 DK 70333-01 (NIDDK)
SOURCE:             Endocrinology, (2007 Jun) Vol. 148, No. 6, pp. 3004-12.
                    Electronic Publication: 2007-03-08.
                    Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:           English
FILE SEGMENT:       Abridged Index Medicus Journals; Priority Journals
```

ENTRY MONTH: 200707
ENTRY DATE: Entered STN: 18 May 2007
Last Updated on STN: 25 Jul 2007
Entered Medline: 24 Jul 2007

ABSTRACT:
Cancer cachexia is a debilitating syndrome of anorexia and loss of lean body mass that accompanies many malignancies. Ghrelin is an orexigenic hormone with a short half-life that has been shown to improve food intake and weight gain in human and animal subjects with cancer cachexia. We used a rat model of cancer cachexia and administered human ghrelin and a synthetic ghrelin analog BIM-28131 via continuous infusion using sc osmotic minipumps. Tumor-implanted rats receiving human ***ghrelin*** or BIM-28131 exhibited a significant increase in food consumption and weight gain vs. saline-treated animals. We used dual-energy x-ray absorptiometry scans to show that the increased weight was due to maintenance of lean mass vs. a loss of lean mass in saline-treated animals. Also, BIM-28131 significantly limited the loss of fat mass normally observed in tumor-implanted rats. We further performed real-time PCR analysis of the hypothalami and brainstems and found that ghrelin-treated animals exhibited a significant increase in expression of orexigenic peptides agouti-related peptide and neuropeptide Y in the hypothalamus and a significant decrease in the expression of IL-1 receptor-I transcript in the hypothalamus and brainstem. We conclude that ghrelin and a synthetic ***ghrelin*** receptor agonist improve weight gain and lean body mass retention via effects involving orexigenic neuropeptides and antiinflammatory changes.

CONTROLLED TERM: Check Tags: Male
Animals
*Body Composition: DE, drug effects
Body Weight: DE, drug effects
*Cachexia: ET, etiology
*Cachexia: PA, pathology
Disease Models, Animal
*Eating: DE, drug effects
Gene Expression Regulation, Neoplastic: DE, drug effects
Growth Hormone: ME, metabolism
Hypothalamus: DE, drug effects
Hypothalamus: ME, metabolism
Insulin-Like Growth Factor I: ME, metabolism
*Neoplasms: CO, complications
Neoplasms: PA, pathology
*Peptide Hormones: PD, pharmacology
Rats
Rats, Inbred F344
Tumor Burden: DE, drug effects

CAS REGISTRY NO.: 67763-96-6 (Insulin-Like Growth Factor I); 9002-72-6 (Growth Hormone)
CHEMICAL NAME: 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 2 OF 66 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2007309573 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17414495
TITLE: Emerging results of anticatabolic therapy with ghrelin.
AUTHOR: Akamizu Takashi; Kangawa Kenji
CORPORATE SOURCE: Ghrelin Research Project, Department of Experimental Therapeutics, Translational Research Center, Kyoto University Hospital, 54 Shogoin-Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan.. akamizu@kuhp.kyoto-u.ac.jp
SOURCE: Current opinion in clinical nutrition and metabolic care,

(2007 May) Vol. 10, No. 3, pp. 278-83. Ref: 58
Journal code: 9804399. ISSN: 1363-1950.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200706
ENTRY DATE: Entered STN: 25 May 2007
Last Updated on STN: 26 Jun 2007
Entered Medline: 25 Jun 2007

ABSTRACT:
PURPOSE OF REVIEW: This review summarizes recent developments in research into anticatabolic therapies with ghrelin. Potential conditions in which ***ghrelin*** treatment may be useful include cachexia, anorexia and ageing. We highlight a number of intriguing basic topics related to the anticatabolic effects of ghrelin. RECENT FINDING: Repeated administration of ***ghrelin*** to patients with congestive heart failure or chronic obstructive pulmonary disease improved appetite, body composition, muscle wasting and functional capacity in open-label pilot studies. An acute, randomized, placebo-controlled, crossover clinical trial of cancer patients with anorexia revealed marked increases in energy intake following treatment. The effects of ghrelin treatment in patients with anorexia nervosa are controversial. Basic research studies have extended our understanding of the upstream regulation of neuropeptide Y/agouti-related protein signalling and the central control of adipocyte metabolism. In addition, alterations in fat-free mass may play a role in ghrelin regulation. SUMMARY: A number of studies are currently evaluating the anticatabolic effects of ***ghrelin*** in the treatment of various diseases, including cachexia, anorexia and age-related disorders. These studies will hopefully lead to the development of novel clinical applications for ghrelin treatment. These studies have also facilitated a better understanding of the molecular basis of the anticatabolic effects of ghrelin.

CONTROLLED TERM: Aging
*Anorexia: DT, drug therapy
Appetite: DE, drug effects
*Cachexia: DT, drug therapy
Data Collection
*Energy Intake: DE, drug effects
*Energy Metabolism: DE, drug effects
Humans
*Peptide Hormones: TU, therapeutic use
CHEMICAL NAME: 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 3 OF 66 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2006120902 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16508225
TITLE: Ghrelin, a novel growth hormone-releasing peptide, in the treatment of cardiopulmonary-associated cachexia.
AUTHOR: Nagaya Noritoshi; Kojima Masakazu; Kangawa Kenji
CORPORATE SOURCE: Department of Regenerative Medicine and Tissue Engineering, National Cardiovascular Center Research Institute, Osaka.
SOURCE: Internal medicine (Tokyo, Japan), (2006) Vol. 45, No. 3, pp. 127-34. Electronic Publication: 2006-03-01. Ref: 83
Journal code: 9204241. E-ISSN: 1349-7235.
COMMENT: Comment in: Intern Med. 2006;45(13):837. PubMed ID: 16880713
PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200608
ENTRY DATE: Entered STN: 2 Mar 2006
Last Updated on STN: 23 Aug 2006
Entered Medline: 22 Aug 2006

ABSTRACT:
Ghrelin is a novel growth hormone (GH)-releasing peptide, isolated from the stomach, which has been identified as an endogenous ligand for GH secretagogue receptor. The discovery of ghrelin indicates that the release of GH from the pituitary might be regulated not only by hypothalamic GH-releasing hormone, but also by ghrelin derived from the stomach. This peptide also stimulates food intake and induces adiposity through GH-independent mechanisms. In addition, ghrelin acts directly on the central nervous system to decrease sympathetic nerve activity. Thus, ***ghrelin*** plays important roles for maintaining GH release and energy homeostasis. Repeated administration of ghrelin improves body composition, muscle wasting, functional capacity, and sympathetic augmentation in cachectic patients with heart failure or chronic obstructive pulmonary disease. These results suggest that ghrelin has anti-cachectic effects through GH-dependent and independent mechanisms. Thus, administration of ghrelin may be a new therapeutic strategy for the treatment of cardiopulmonary-associated cachexia.

CONTROLLED TERM: Animals
*Cachexia: DT, drug therapy
Cachexia: ET, etiology
*Growth Hormone: TU, therapeutic use
*Heart Failure, Congestive: CO, complications
Heart Failure, Congestive: PP, physiopathology
Humans
Peptide Hormones: PD, pharmacology
Peptide Hormones: PH, physiology
*Peptide Hormones: TU, therapeutic use
*Pulmonary Disease, Chronic Obstructive: CO, complications
Pulmonary Disease, Chronic Obstructive: PP, physiopathology
Stomach: ME, metabolism
CAS REGISTRY NO.: 9002-72-6 (Growth Hormone)
CHEMICAL NAME: 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 4 OF 66 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2005491621 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16162705
TITLE: Treatment of cachexia with ghrelin in patients with COPD.
AUTHOR: Nagaya Noritoshi; Itoh Takefumi; Murakami Shinsuke; Oya Hideo; Uematsu Masaaki; Miyatake Kunio; Kangawa Kenji
CORPORATE SOURCE: Department of Internal Medicine, National Cardiovascular Center, 5-7-1 Fujishirodai, Suita, Osaka 565-8565, Japan.. nnagaya@ri.ncvc.go.jp
SOURCE: Chest, (2005 Sep) Vol. 128, No. 3, pp. 1187-93.
Journal code: 0231335. ISSN: 0012-3692.
COMMENT: Comment in: Chest. 2005 Sep;128(3):1084-6. PubMed ID: 16162686
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200511
ENTRY DATE: Entered STN: 16 Sep 2005
Last Updated on STN: 9 Nov 2005
Entered Medline: 8 Nov 2005

ABSTRACT:
STUDY OBJECTIVES: Ghrelin is a novel growth hormone (GH)-releasing peptide that also induces a positive energy balance by decreasing fat utility and stimulating feeding through GH-independent mechanisms. We investigated whether ghrelin improves cachexia and functional capacity in patients with COPD. METHODS: This is an open-label pilot study. Human ghrelin (2 microg/kg bid) was IV administered to seven cachectic patients with COPD for 3 weeks. Food intake, body composition, muscle strength, exercise capacity, pulmonary function, and sympathetic nerve activity were examined before and after ghrelin therapy. RESULTS: A single administration of ***ghrelin*** markedly increased serum GH (21-fold). Three-week treatment with ghrelin resulted in a significant increase in mean (+/- SEM) body weight (49.3 +/- 3.6 to 50.3 +/- 3.8 kg; $p < 0.05$). Food intake was significantly increased during ghrelin therapy. Ghrelin increased lean body mass and peripheral and respiratory muscle strength. ***Ghrelin*** significantly increased Karnofsky performance status score and the distance walked in 6 min (370 +/- 30 to 432 +/- 35 m; $p < 0.05$), although it did not significantly alter pulmonary function. Ghrelin attenuated the exaggerated sympathetic nerve activity, as indicated by a marked decrease in plasma norepinephrine level (889 +/- 123 to 597 +/- 116 pg/mL; $p < 0.05$). CONCLUSIONS: These preliminary results suggest that repeated administration of ghrelin improves body composition, muscle wasting, functional capacity, and sympathetic augmentation in cachectic patients with COPD.

CONTROLLED TERM: Check Tags: Female; Male
Aged
Aged, 80 and over
Body Composition: DE, drug effects
*Cachexia: DT, drug therapy
Cachexia: ET, etiology
Exercise Tolerance: DE, drug effects
Growth Hormone-Releasing Hormone: PD, pharmacology
*Growth Hormone-Releasing Hormone: TU, therapeutic use
Humans
Muscle Weakness: DT, drug therapy
Muscular Atrophy: DT, drug therapy
Peptide Hormones: PD, pharmacology
*Peptide Hormones: TU, therapeutic use
Pilot Projects
*Pulmonary Disease, Chronic Obstructive: CO, complications
Recovery of Function: DE, drug effects
Respiratory Function Tests
Respiratory System: DE, drug effects
Sympathetic Nervous System: DE, drug effects
CAS REGISTRY NO.: 9034-39-3 (Growth Hormone-Releasing Hormone)
CHEMICAL NAME: 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 5 OF 66 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2003164275 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12681236
TITLE: Ghrelin improves left ventricular dysfunction and cardiac cachexia in heart failure.
AUTHOR: Nagaya Noritoshi; Kangawa Kenji
CORPORATE SOURCE: Department of Internal Medicine, National Cardiovascular Center, 5-7-1 Fujishirodai, Suita, Osaka, 565-8565, Japan..

nagayann@hsp.ncvc.go.jp
SOURCE: Current opinion in pharmacology, (2003 Apr) Vol. 3, No. 2, pp. 146-51. Ref: 55
Journal code: 100966133. ISSN: 1471-4892.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 9 Apr 2003
Last Updated on STN: 28 Aug 2003
Entered Medline: 27 Aug 2003

ABSTRACT:
Ghrelin is a novel growth-hormone-releasing peptide isolated from the stomach that has been identified as an endogenous ligand for the growth-hormone secretagogue receptor. This peptide results in a positive energy balance by stimulating food intake and inducing adiposity through growth-hormone-independent mechanisms. In addition, ghrelin has several cardiovascular effects, as indicated by the presence of its receptor in blood vessels and ventricles of the heart. Infusion of ghrelin decreases systemic vascular resistance and increases cardiac output in patients with heart failure. Furthermore, repeated administration of ghrelin improves cardiac structure and function, and attenuates the development of cardiac cachexia in rats with heart failure. These results suggest that ***ghrelin*** has therapeutic potential in the treatment of severe chronic heart failure.

CONTROLLED TERM: Animals
Cachexia: BL, blood
*Cachexia: DT, drug therapy
Heart Failure, Congestive: BL, blood
*Heart Failure, Congestive: DT, drug therapy
Humans
Peptide Hormones: BL, blood
Peptide Hormones: SE, secretion
*Peptide Hormones: TU, therapeutic use
Ventricular Dysfunction, Left: BL, blood
*Ventricular Dysfunction, Left: DT, drug therapy
CHEMICAL NAME: 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 6 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2007011711 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17030099
TITLE: Ghrelin may reduce radiation-induced mucositis and anorexia in head-neck cancer.
AUTHOR: Guney Yildiz; Ozel Turkcu Ummuhani; Hicsonmez Ayse; Nalca Andrieu Meltem; Kurtman Cengiz
CORPORATE SOURCE: Department of Radiation Oncology, Ankara University School of Medicine, Cebeci Hospital, Dikimevi, Ankara 06590, Turkey.. yildiz_guney@yahoo.com
SOURCE: Medical hypotheses, (2007) Vol. 68, No. 3, pp. 538-40.
Electronic Publication: 2006-10-09.
Journal code: 7505668. ISSN: 0306-9877.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200704
ENTRY DATE: Entered STN: 9 Jan 2007

Last Updated on STN: 6 Apr 2007
Entered Medline: 5 Apr 2007

ABSTRACT:
Body weight loss is common in cancer patients, and is often associated with poor prognosis, it greatly impairs quality of life (QOL). Radiation therapy (RT) is used in head and neck cancers (HNC) either as a primary treatment or as an adjuvant therapy to surgery. Patients with HNC are most susceptible to malnutrition especially due to anorexia, which is aggravated by RT. Multiple pro-inflammatory cytokines, such as interleukin-6 (IL-6), interleukin-1beta (IL-1beta), interferon (IFN)-gamma and tumor necrosis factor-alpha(TNF-alpha), have been all associated with the development of both anorexia and oral mucositis. Radiation-induced mucositis occurs in almost all patients, who are treated for HNC, it could also cause weight loss. Ghrelin is a novel 28-amino acid peptide, which up-regulates body weight through appetite control, increase food intake, down-regulate energy expenditure and induces adiposity. Furthermore, ghrelin inhibits pro-inflammatory cytokines such as IL-1alpha, IL-1beta, TNF-alpha which may cause oral mucositis and aneroxia, which are the results of weight loss. Thus weight loss during RT is an early indicator of nutritional decline, we propose that recombinant ghrelin used prophylactically could be useful as an appetite stimulant; and preventive of mucositis because of its anti-inflammatory effect, it might help patients maintain weight over the course of curative RT of the HNC and can improve specific aspects of QOL. This issue warrants further studies.

CONTROLLED TERM: Anorexia: PC, prevention & control
*Anorexia: RI, radionuclide imaging
Appetite
Head and Neck Neoplasms: PP, physiopathology
*Head and Neck Neoplasms: RT, radiotherapy
Humans
*Mucositis: DT, drug therapy
*Mucositis: RI, radionuclide imaging
*Peptide Hormones: TU, therapeutic use
*Radiotherapy: AE, adverse effects
CHEMICAL NAME: 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 7 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2006463117 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16880713
TITLE: Ghrelin and neurohumoral antagonists in the treatment of cachexia associated with cardiopulmonary disease.
AUTHOR: Lainscak Mitja; Andreas Stefan; Scanlon Paul D; Somers Virend K; Anker Stefan D
SOURCE: Internal medicine (Tokyo, Japan), (2006) Vol. 45, No. 13, pp. 837. Electronic Publication: 2006-08-01.
Journal code: 9204241. E-ISSN: 1349-7235.
COMMENT: Comment on: Intern Med. 2006 Mar;45(3):127-34. PubMed ID: 16508225
PUB. COUNTRY: Japan
DOCUMENT TYPE: Commentary
Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200609
ENTRY DATE: Entered STN: 5 Aug 2006
Last Updated on STN: 16 Sep 2006
Entered Medline: 15 Sep 2006
CONTROLLED TERM: *Cachexia: DT, drug therapy
Cachexia: ET, etiology
Heart Failure, Congestive: CO, complications

Humans
*Peptide Hormones: TU, therapeutic use
Pulmonary Disease, Chronic Obstructive: CO, complications
CHEMICAL NAME: 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 8 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2006260324 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16685441
TITLE: Effects of ghrelin on anorexia in tumor-bearing mice with eicosanoid-related cachexia.
AUTHOR: Wang Wenhua; Andersson Marianne; Iresjo Britt-Marie; Lonnroth Christina; Lundholm Kent
CORPORATE SOURCE: Surgical Metabolic Research Laboratory at Lundberg Laboratory for Cancer Research, Department of Surgery, Sahlgrenska University Hospital, Goteborg University, Goteborg, Sweden.
SOURCE: International journal of oncology, (2006 Jun) Vol. 28, No. 6, pp. 1393-400.
Journal code: 9306042. ISSN: 1019-6439.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200608
ENTRY DATE: Entered STN: 11 May 2006
Last Updated on STN: 17 Aug 2006
Entered Medline: 16 Aug 2006

ABSTRACT:
Ghrelin is a novel brain-gut peptide that stimulates food intake and may secondarily increase body weight via a growth hormone secretagogue receptor (GHS-R). Tumor-bearing mice (MCG101), characterized by anorexia, fat loss and muscle wasting due to increased concentration of PGE2 and proinflammatory cytokines (IL-1beta, IL-6, TNF-alpha), were provided ghrelin i.p. at a low (20 microg/day) and high dose (40 microg/day) to examine the ability of ***ghrelin*** to counteract tumor-induced anorexia. Immunohistochemical staining and Western blot analyses were used to identify GHS-R expression in the brain as well as its relationship to NPY expression in hypothalamic neurons. GHS-R mRNA in hypothalamus and ghrelin mRNA in gastric fundus were quantified by RT-PCR. Body composition was determined by carcass extractions. GHS-R expression in hypothalamus and plasma ghrelin levels were significantly increased in freely-fed tumor-bearing mice, while gastric fundus expression of ghrelin was unaltered compared to non-tumor-bearing mice (controls). Ghrelin treatment increased food intake, body weight and whole body fat at both low and high doses of ***ghrelin*** in normal controls, while tumor-bearing mice showed improved intake and body composition at the high dose of ghrelin only. Exogenous ghrelin normalized the GHS-R expression in hypothalamus from tumor-bearing mice without alterations in the gastric fundus expression of ***ghrelin.*** Tumor growth was not altered by exogenous ghrelin. Our results indicate that MCG 101-bearing mice became ghrelin resistant despite upregulation of hypothalamic GHS-R expression, which confirms similar indirect observations in cancer patients. Thus, other factors downstream of the ghrelin-GHS-R system appear to be more important than ghrelin to explain cancer-induced anorexia.

CONTROLLED TERM: Check Tags: Female
Animals
*Anorexia: DT, drug therapy
Anorexia: ET, etiology
*Cachexia: DT, drug therapy

Cachexia: ET, etiology
*Eicosanoids: AE, adverse effects
Energy Intake
Growth Hormone: TU, therapeutic use
Mice
Mice, Inbred C57BL
*Peptide Hormones: TU, therapeutic use
RNA, Messenger: GE, genetics
Receptors, G-Protein-Coupled: GE, genetics
Reverse Transcriptase Polymerase Chain Reaction
Sarcoma, Experimental: CO, complications
*Sarcoma, Experimental: PA, pathology
CAS REGISTRY NO.: 9002-72-6 (Growth Hormone)
CHEMICAL NAME: 0 (Eicosanoids); 0 (Peptide Hormones); 0 (RNA, Messenger); 0 (Receptors, G-Protein-Coupled); 0 (ghrelin); 0 (growth hormone secretagogue receptor)

L99 ANSWER 9 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2006638415 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16873986
TITLE: Translational research on the clinical applications of ghrelin.
AUTHOR: Akamizu Takashi; Kangawa Kenji
CORPORATE SOURCE: Ghrelin Research Project, Department of Experimental Therapeutics, Translational Research Center, Kyoto University Hospital, Kyoto University School of Medicine, Kyoto, Japan.
SOURCE: Endocrine journal, (2006 Oct) Vol. 53, No. 5, pp. 585-91.
Electronic Publication: 2006-07-28. Ref: 52
Journal code: 9313485. ISSN: 0918-8959.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200704
ENTRY DATE: Entered STN: 1 Nov 2006
Last Updated on STN: 3 Apr 2007
Entered Medline: 2 Apr 2007
CONTROLLED TERM: Anorexia Nervosa: DT, drug therapy
Cachexia: DT, drug therapy
*Clinical Trials
Clinical Trials, Phase I
Clinical Trials, Phase II
Dwarfism, Pituitary: DT, drug therapy
Eating Disorders: DT, drug therapy
Humans
Models, Biological
Peptide Hormones: PH, physiology
*Peptide Hormones: TU, therapeutic use
CHEMICAL NAME: 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 10 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2006151694 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16541004
TITLE: Role of ghrelin in the regulation of appetite in children.
AUTHOR: Savastio S; Bellone S; Baldelli R; Ferraris M; Lapidari A; Zanetta F; Sogni S; Petri A; Bona G
CORPORATE SOURCE: Division of Pediatrics, Department of Medical Sciences,

University of Piemonte Orientale, A. Avogadro, Novara, Italy.
SOURCE: Minerva pediatrica, (2006 Feb) Vol. 58, No. 1, pp. 21-6. Ref: 47
Journal code: 0400740. ISSN: 0026-4946.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200608
ENTRY DATE: Entered STN: 17 Mar 2006
Last Updated on STN: 2 Aug 2006
Entered Medline: 1 Aug 2006

ABSTRACT:
Ghrelin, the new recently discovered hormone, is a 28 amino-acid acylated peptide predominantly produced by the stomach characterized by a strong GH-releasing activity mediated by the hypothalamic-pituitary GH secretagogues (GHSs) receptors. Ghrelin and GHSs, acting on central and peripheral receptors, exert other actions such as stimulation of ACTH and prolactin secretion, influence on insulin secretion and glucose metabolism, orexigenic effect and modulatory activity on the neuroendocrine and metabolic response to starvation, influence on exocrine gastro-entero-pancreatic functions, cardiovascular activities and modulation of cell proliferation and apoptosis. The wide spectrum of ghrelin action requires further studies to provide critical information on the role of ghrelin and the potential perspectives of its analogues in the clinical practice. This point is of particular interest in the field of pediatric endocrinology and metabolism because the ghrelin story started focusing on GH deficiency and is now extending to aspects that once again are of major relevance such as obesity and eating disorders, regulation of the hypothalamus-pituitary-adrenal and gonadal axis. More studies are needed to evaluate the real impact of ghrelin in different non endocrine processes and the possible use of ghrelin analogues in different diseases condition.

CONTROLLED TERM:
*Appetite: DE, drug effects
*Appetite Regulation: DE, drug effects
Child
Eating Disorders: DT, drug therapy
Eating Disorders: ME, metabolism
Human Growth Hormone: PD, pharmacology
Human Growth Hormone: TU, therapeutic use
Humans
*Peptide Hormones: PD, pharmacology
*Peptide Hormones: TU, therapeutic use
Treatment Outcome
CAS REGISTRY NO.: 12629-01-5 (Human Growth Hormone)
CHEMICAL NAME: 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 11 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2005651221 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16332313
TITLE: Cachexia in chronic heart failure: prognostic implications and novel therapeutic approaches.
AUTHOR: Akashi Yoshihiro J; Springer Jochen; Anker Stefan D
CORPORATE SOURCE: Division of Applied Cachexia Research, Department of Cardiology, Charite Campus Virchow-Klinikum, Augustenburger Platz 1, 13353 Berlin, Germany.
SOURCE: Current heart failure reports, (2005 Dec) Vol. 2, No. 4, pp. 198-203. Ref: 58
Journal code: 101196487. ISSN: 1546-9530.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200602
ENTRY DATE: Entered STN: 16 Dec 2005
Last Updated on STN: 28 Feb 2006
Entered Medline: 23 Feb 2006

ABSTRACT:
Cachexia in patients with chronic heart failure (CHF) has been recognized for a long time; however, it has not received much attention until recently. Cardiac cachexia, a common and serious complication of CHF, is associated with very poor prognosis. Several studies have demonstrated that increased neurohormonal and immune abnormalities may play a crucial role in the pathophysiology of cardiac cachexia. Hormonal and catabolic/anabolic imbalances of the body are likely to be responsible for the development of cachexia in CHF. Recently, ***ghrelin*** , a novel growth hormone-releasing peptide, has been widely noticed to have potential in the treatment of severe CHF and cardiac cachexia. However, further research will be necessary to identify the exact pathways involved and to find the best therapeutic strategies of using ghrelin to fight the wasting process.

CONTROLLED TERM:
Cachexia: DT, drug therapy
*Cachexia: ET, etiology
Cachexia: ME, metabolism
Disease Progression
*Growth Hormone: ME, metabolism
*Heart Failure, Congestive: CO, complications
Humans
*Peptide Hormones: TU, therapeutic use
Prognosis
CAS REGISTRY NO.: 9002-72-6 (Growth Hormone)
CHEMICAL NAME: 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 12 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2007263516 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17471875
TITLE: [Secondary anorexia: physiology and treatment].
Anorexia secundaria: fisiologia y tratamiento.
AUTHOR: Milke Garcia Maria del Pilar -
CORPORATE SOURCE: Coordinadora de Investigacion y Servicio Social en Nutricion.
SOURCE: Revista de gastroenterologia de Mexico, (2005 Nov) Vol. 70 Suppl 3, pp. 94-5. Ref: 8
Journal code: 0404271. ISSN: 0375-0906.
PUB. COUNTRY: Mexico
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Spanish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200705
ENTRY DATE: Entered STN: 3 May 2007
Last Updated on STN: 15 May 2007
Entered Medline: 14 May 2007

CONTROLLED TERM:
Anorexia: DT, drug therapy
*Anorexia: ET, etiology
Anorexia: PP, physiopathology
*Anorexia: TH, therapy
Anti-Inflammatory Agents: TU, therapeutic use
Cachexia: CO, complications

Chronic Disease
*Gastrointestinal Diseases: CO, complications
Humans
Peptide Hormones: TU, therapeutic use
Steroids: TU, therapeutic use
CHEMICAL NAME: 0 (Anti-Inflammatory Agents); 0 (Peptide Hormones); 0 (Steroids); 0 (ghrelin)

L99 ANSWER 13 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2004621114 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15569841
TITLE: Effects of ghrelin administration on left ventricular function, exercise capacity, and muscle wasting in patients with chronic heart failure.
AUTHOR: Nagaya Noritoshi; Moriya Junji; Yasumura Yoshio; Uematsu Masaaki; Ono Fumiaki; Shimizu Wataru; Ueno Kazuyuki; Kitakaze Masafumi; Miyatake Kunio; Kangawa Kenji
CORPORATE SOURCE: Department of Internal Medicine, National Cardiovascular Center, 5-7-1 Fujishirodai, Suita, Osaka 565-8565, Japan.. nagayann@hsp.ncvc.go.jp
SOURCE: Circulation, (2004 Dec 14) Vol. 110, No. 24, pp. 3674-9. Electronic Publication: 2004-11-29. Journal code: 0147763. E-ISSN: 1524-4539.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200505
ENTRY DATE: Entered STN: 20 Dec 2004 Last Updated on STN: 26 May 2005 Entered Medline: 25 May 2005

ABSTRACT:
BACKGROUND: Ghrelin is a novel growth hormone-releasing peptide that also induces vasodilation, inhibits sympathetic nerve activity, and stimulates feeding through growth hormone-independent mechanisms. We investigated the effects of ghrelin on left ventricular (LV) function, exercise capacity, and muscle wasting in patients with chronic heart failure (CHF). METHODS AND RESULTS: Human synthetic ghrelin (2 microg/kg twice a day) was intravenously administered to 10 patients with CHF for 3 weeks. Echocardiography, cardiopulmonary exercise testing, dual x-ray absorptiometry, and blood sampling were performed before and after ghrelin therapy. A single administration of ghrelin elicited a marked increase in serum GH (25-fold). Three-week administration of ghrelin resulted in a significant decrease in plasma norepinephrine (1132+/-188 to 655+/-134 pg/mL; P<0.001). Ghrelin increased LV ejection fraction (27+/-2% to 31+/-2%; P<0.05) in association with an increase in LV mass and a decrease in LV end-systolic volume. Treatment with ghrelin increased peak workload and peak oxygen consumption during exercise. Ghrelin improved muscle wasting, as indicated by increases in muscle strength and lean body mass. These parameters remained unchanged in 8 patients with CHF who did not receive ghrelin therapy. CONCLUSIONS: These preliminary results suggest that repeated administration of ghrelin improves LV function, exercise capacity, and muscle wasting in patients with CHF.

CONTROLLED TERM: Check Tags: Female; Male
Aged
Aged, 80 and over
Body Weight: DE, drug effects
*Cachexia: DT, drug therapy

Cachexia: ET, etiology
Cachexia: PP, physiopathology
Chronic Disease
Eating: DE, drug effects
*Exercise
Heart Failure, Congestive: CO, complications
*Heart Failure, Congestive: DT, drug therapy
Heart Failure, Congestive: PP, physiopathology
Hemodynamic Processes
Human Growth Hormone: BL, blood
Humans
Infusions, Intravenous
Middle Aged
Oxygen Consumption: DE, drug effects
Peptide Hormones: AD, administration & dosage
Peptide Hormones: AE, adverse effects
*Peptide Hormones: TU, therapeutic use
Pulmonary Ventilation: DE, drug effects
Sympathetic Nervous System: DE, drug effects
Sympathetic Nervous System: PP, physiopathology
Ventricular Function, Left: DE, drug effects
CAS REGISTRY NO.: 12629-01-5 (Human Growth Hormone)
CHEMICAL NAME: 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 14 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2004599327 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15572207
TITLE: Regulation of ghrelin gene expression in stomach and feeding response to a ghrelin analogue in two strains of rats.
AUTHOR: Liu Xiaotuan; York David A; Bray George A
CORPORATE SOURCE: Experimental Obesity Laboratory, Pennington Biomedical Research Center, 6400 Perkins Road, Baton Rouge, LA 70808, USA.. liux@pbrc.edu
SOURCE: Peptides, (2004 Dec) Vol. 25, No. 12, pp. 2171-7. Journal code: 8008690. ISSN: 0196-9781.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 2 Dec 2004 Last Updated on STN: 8 Jun 2005 Entered Medline: 7 Jun 2005

ABSTRACT:
Ghrelin is a peptide produced by the stomach and released into the circulation. As a natural ligand of the growth hormone secretagogue (GHS) receptor, it stimulates growth hormone secretion but it also stimulates feeding in humans and rodents. The orexigenic effect of ghrelin has been related to AgRP/NPY and orexin pathways. We proposed that ghrelin might be involved in the susceptibility to diet induced obesity and in the regulation of macronutrient selection. We have investigated these hypotheses in two strains of rat, the Osborne-Mendel (OM) rat that prefers diets high in fat and is sensitive to dietary obesity and the S5B/Pl (S5B) rat that prefers a low fat diet and is resistant to high fat diet induced obesity. OM and S5B rats were adapted to a choice of high fat (HF) and low fat (LF) diet for 2 weeks. GHRP-2, an ***analogue*** of ghrelin, was injected intraperitoneally into satiated and 24 h fasted rats at doses of 10, 30 and 90 nmol. Food intake was measured over the next 4 h period. In satiated S5B rats, GHRP-2 stimulated

intake of the LF diet in a dose dependent manner but did not affect the intake of the HF diet. In satiated OM rats, 90 nmol of GHRP-2 stimulated HF intake. In contrast, neither fasted OM nor S5B rats increased the intake of either HF or LF diet in response to GHRP-2. Fasting for 18 h induced a large rise in ghrelin mRNA in stomach of OM rats but not in S5B rats. There were no significant differences in plasma total ghrelin. An increase in ghrelin mRNA in stomach immediately before the onset of the dark cycle was observed in OM but not in S5B rats. Active ghrelin level was significantly affected by different feeding conditions in both OM and S5B rats adapted on HF diet with a trend to increase after 48 h of fasting and to decline to basal levels following 10 h of refeeding. These data suggest that ghrelin stimulates the intake of the preferred macronutrient. In addition, a differential regulation of ghrelin gene expression between OM and S5B rats may be important in their differential sensitivity to HF diet-induced obesity.

CONTROLLED TERM: Check Tags: Male
Animals
Dietary Fats: AD, administration & dosage
*Eating
Eating: DE, drug effects
Energy Intake: DE, drug effects
Fasting: ME, metabolism
*Gene Expression-Regulation
*Oligopeptides: PD, pharmacology
Peptide Hormones: BI, biosynthesis
Peptide Hormones: BL, blood
*Peptide Hormones: GE, genetics
Rats
*Stomach: ME, metabolism

CHEMICAL NAME: 0 (Dietary Fats); 0 (Oligopeptides); 0 (Peptide Hormones); 0 (ghrelin); 0 (growth hormone-releasing peptide-2)

L99 ANSWER 15 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2004114490 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15004432
TITLE: Orexigenic actions of ghrelin in goldfish: feeding-induced changes in brain and gut mRNA expression and serum levels, and responses to central and peripheral injections.
AUTHOR: Unniappan Suraj; Canosa Luis Fabian; Peter Richard E
CORPORATE SOURCE: Department of Biological Sciences, University of Alberta, Edmonton, Alta., Canada.
SOURCE: Neuroendocrinology, (2004 Feb) Vol. 79, No. 2, pp. 100-8.
Journal code: 0035665. ISSN: 0028-3835.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 9 Mar 2004
Last Updated on STN: 18 May 2004
Entered Medline: 17 May 2004

ABSTRACT:
In this study, we examined (i) the preprandial, postprandial and starvation-induced changes in the preproghrelin mRNA expression and serum ghrelin levels, and (ii) the effects of intracerebroventricular and intraperitoneal administration of ghrelin on food intake in goldfish. Slot blot analysis revealed a significant postprandial decrease in preproghrelin mRNA expression in the hypothalamus (1 and 3 h after feeding) and gut (3 h after feeding). A similar postprandial decrease (1 and 3 h after feeding) in

serum ghrelin levels was also detected. In the fish that were unfed at the regular feeding time, the hypothalamic preproghrelin mRNA expression and the serum ghrelin levels remained unchanged, while the preproghrelin mRNA expression in the gut decreased 3 h after the regular feeding time. Starvation increased preproghrelin mRNA expression in the hypothalamus and gut on the 7th day. Serum ghrelin levels were significantly elevated on days 3 and 5 of starvation. Intracerebroventricular injections of n-octanoylated ***ghrelin*** -like peptides (gGRL([1-12])) (10 ng/g body weight) and human ghrelin (1 and 10 ng/g body weight) and intraperitoneal injections of n-octanoylated gGRL([1-12]) (10 ng/g body weight), gGRL([1-19]) (100 ng/g body weight) and human ghrelin (10 and 100 ng/g body weight) stimulated food intake in goldfish. The patterns of synthesis, secretion and actions indicate that ghrelin is an orexigen in goldfish.

CONTROLLED TERM: Check Tags: Female; Male
Animals
*Appetite: PH, physiology
*Digestive System: ME, metabolism
Eating: PH, physiology
*Feeding Behavior: PH, physiology
*Goldfish: PH, physiology
Growth Hormone: PH, physiology
*Hypothalamus: ME, metabolism
Peptide Hormones: GE, genetics
Peptide Hormones: ME, metabolism
*Peptide Hormones: PH, physiology
Postprandial Period
Protein Precursors: GE, genetics
Protein Precursors: ME, metabolism
RNA, Messenger: AN, analysis
Starvation: GE, genetics
Starvation: ME, metabolism

CAS REGISTRY NO.: 9002-72-6 (Growth Hormone)
CHEMICAL NAME: 0 (Peptide Hormones); 0 (Protein Precursors); 0 (RNA, Messenger); 0 (ghrelin)

L99 ANSWER 16 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2004434142 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15339248
TITLE: Novel analogs of ghrelin: physiological and clinical implications.
AUTHOR: Halem Heather A; Taylor John E; Dong Jesse Z; Shen Yeelana; Datta Rakesh; Abizaid Alfonso; Diano Sabrina; Horvath Tamas; Zizzari Philippe; Bluet-Pajot Marie-Therese; Epelbaum Jacques; Culler Michael D
CORPORATE SOURCE: IPSEN, 27 Maple Street, Milford, Massachusetts 01757, USA.
SOURCE: European journal of endocrinology / European Federation of Endocrine Societies, (2004 Aug) Vol. 151 Suppl 1, pp. S71-5.
Journal code: 9423848. ISSN: 0804-4643.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 2 Sep 2004
Last Updated on STN: 17 Oct 2004
Entered Medline: 15 Oct 2004

ABSTRACT:
Ghrelin, the 28 amino acid peptide recently identified as the natural ligand

for the growth hormone (GH) secretagogue (GHS) receptor, has multiple activities in addition to stimulation of GH secretion, including stimulation of feeding and weight gain. To utilize these actions for potential therapeutic benefit, we have produced analogs of human ghrelin with enhanced metabolic stability, affinity for the GHS receptor, and efficacy in stimulating weight gain. We have also discovered an analog of ghrelin, BIM-28163, that is an antagonist at the GHS receptor and that fully inhibits GHS receptor activation induced by native ghrelin. In vivo, BIM-28163 does not increase GH secretion but fully blocks ghrelin-induced GH secretion. In contrast, BIM-28163 acts as a full agonist with regard to the ghrelin actions of stimulating weight gain and food intake. These results suggest that a receptor other than the GHS receptor mediates the actions of ghrelin on feeding and weight gain. This concept is strengthened by our observation that at certain hypothalamic sites, BIM-28163 acts as an antagonist of ghrelin-induced neuronal activation, while at other sites, both ghrelin and BIM-28163 induce neuronal activation via the same receptor. Collectively, these results indicate the existence of a novel ghrelin receptor that may regulate the feeding activity of ghrelin. Using BIM-28163 as a tool to define the endogenous role of ghrelin in normal GH secretion, we have demonstrated that antagonism of the GHS receptor in normal rats does not impair the pulsatility of GH secretion but lowers the pulse amplitude and mean GH level. These results demonstrate that endogenous ghrelin acts to amplify the basic pattern of GH secretion established by the interplay of hypothalamic GH-releasing hormone and somatostatin. These studies demonstrate the feasibility of creating ghrelin analogs that are selective for specific activities, as well as their utility in dissecting the role of ghrelin in both normal physiology and specific pathologies.

CONTROLLED TERM: Check Tags: Male
Animals
Eating: DE, drug effects
Growth Hormone: SE, secretion
Humans
*Peptide Hormones: AI, antagonists & inhibitors
*Peptide Hormones: PD, pharmacology
*Peptide Hormones: PH, physiology
Peptide Hormones: TU, therapeutic use
Rats
*Receptors, G-Protein-Coupled: AI, antagonists & inhibitors
Weight Gain: DE, drug effects

CAS REGISTRY NO.: 9002-72-6 (Growth Hormone)

CHEMICAL NAME: 0 (BIM28163); 0 (Peptide Hormones); 0 (Receptors, G-Protein-Coupled); 0 (ghrelin); 0 (growth hormone secretagogue receptor)

L99 ANSWER 17 OF 66 MEDLINE on STN

ACCESSION NUMBER: 2003566796 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12960078

TITLE: Alterations of plasma ghrelin levels in rats with lipopolysaccharide-induced wasting syndrome and effects of ghrelin treatment on the syndrome.

AUTHOR: Hataya Yuji; Akamizu Takashi; Hosoda Hiroshi; Kanamoto Naotetsu; Moriyama Kenji; Kangawa Kenji; Takaya Kazuhiko; Nakao Kazuwa

CORPORATE SOURCE: Department of Medicine and Clinical Science, Kyoto University Graduate School of Medicine, Kyoto 606-8507, Japan.

SOURCE: Endocrinology, (2003 Dec) Vol. 144, No. 12, pp. 5365-71. Electronic Publication: 2003-08-28. Journal code: 0375040. ISSN: 0013-7227.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200401

ENTRY DATE: Entered STN: 16 Dec 2003
Last Updated on STN: 6 Jan 2004
Entered Medline: 5 Jan 2004

ABSTRACT:

Ghrelin not only strongly stimulates GH secretion, but is also involved in energy homeostasis by stimulating food intake and promoting adiposity through a GH-independent mechanism. These effects of ghrelin may play an important role in the pathophysiology of inflammatory wasting syndrome, in which both the somatotropic axis and energy balance are altered. In this study we investigated plasma ghrelin concentrations after lipopolysaccharide (LPS) administration to rats, a model of the wasting syndrome and critical illness. In addition, the therapeutic potential of the antiwasting effects of ghrelin was explored using LPS-injected rats. A single LPS injection suppressed plasma ghrelin levels 6 and 12 h later. Maximal reduction was observed 12 h after LPS injection, in a dose-dependent manner. In contrast, plasma ghrelin levels were elevated after repeated LPS injections on d 2 and 5. Peripheral administration of ghrelin twice daily (10 nmol/rat) for 5 d increased body weight gain in repeated LPS-injected rats. Furthermore, both adipose tissue weight and plasma leptin concentrations were increased after ghrelin administration in these rats. In conclusion, plasma ghrelin levels are altered in LPS-injected rats, and ghrelin treatment may provide a new therapeutic approach to the wasting syndrome and critical illness.

CONTROLLED TERM: Check Tags: Male
Adipose Tissue: AH, anatomy & histology
Adipose Tissue: DE, drug effects
Animals
Eating: DE, drug effects
Leptin: BL, blood
Lipopolysaccharides
Organ Size: DE, drug effects
*Peptide Hormones: BL, blood
*Peptide Hormones: PD, pharmacology
Radioimmunoassay
Rats
Rats, Wistar
Spleen: AH, anatomy & histology
Spleen: DE, drug effects
*Wasting Syndrome: BL, blood
Wasting Syndrome: CI, chemically induced
*Wasting Syndrome: DT, drug therapy

CHEMICAL NAME: 0 (Leptin); 0 (Lipopolysaccharides); 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 18 OF 66 MEDLINE on STN

ACCESSION NUMBER: 2003411230 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12951072

TITLE: Ghrelin promotes pancreatic adenocarcinoma cellular proliferation and invasiveness.

AUTHOR: Duxbury Mark S; Waseem Talat; Ito Hiromichi; Robinson Malcolm K; Zinner Michael J; Ashley Stanley W; Whang Edward E

CORPORATE SOURCE: Department of Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA.

CONTRACT NUMBER: DK 02786 (NIDDK)
DK 47326 (NIDDK)

SOURCE: Biochemical and biophysical research communications, (2003 Sep 19) Vol. 309, No. 2, pp. 464-8. Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY) Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 3 Sep 2003
Last Updated on STN: 1 Nov 2003
Entered Medline: 31 Oct 2003

ABSTRACT:
Ghrelin, a newly described potent orexigenic peptide, may have therapeutic potential in patients with cachexia. We assessed whether pancreatic adenocarcinoma, commonly associated with marked cachexia, is a ***ghrelin*** -responsive malignancy. Pancreatic adenocarcinoma cells were exposed to ghrelin (0-100 nM). Proliferation was determined by MTT assay. Ghrelin, ghrelin 1a and 1b receptor expression and Akt phosphorylation were assessed. The effects of ghrelin (+/- its antagonist D-Lys-GHRP6, or the PI3-K inhibitor Wortmannin) on cellular motility and invasiveness were quantified by Matrigel Boyden chamber assay. All cell lines expressed ghrelin 1a and 1b receptor transcript and protein, but only PANC1 weakly expressed ghrelin transcript. Ten nanomolar ***ghrelin*** increased proliferation, motility, invasiveness, and Akt phosphorylation in all cell lines. Proliferation was affected dose-dependently, being suppressed at higher ghrelin concentrations. D-Lys-GHRP6 suppressed ghrelin-induced proliferation, invasion, and Akt phosphorylation. Wortmannin abolished the effects of ghrelin on motility and invasiveness. Pancreatic adenocarcinoma is a ghrelin -responsive malignancy.

CONTROLLED TERM:
Adenocarcinoma: CO, complications
*Adenocarcinoma: PA, pathology
Androstadienes: PD, pharmacology
Cachexia: DT, drug therapy
Cachexia: ET, etiology
Cell Division: DE, drug effects
Dose-Response Relationship, Drug
Neoplasm Invasiveness
Pancreatic Neoplasms: CO, complications
*Pancreatic Neoplasms: PA, pathology
*Peptide Hormones: PD, pharmacology
Peptide Hormones: TU, therapeutic use
Tumor Cells, Cultured: DE, drug effects
Tumor Cells, Cultured: ME, metabolism
Tumor Cells, Cultured: PA, pathology

CAS REGISTRY NO.: 19545-26-7 (wortmannin)
CHEMICAL NAME: 0 (Androstadienes); 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 19 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2003055497 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12565855
TITLE: Anti-cachectic effect of ghrelin in nude mice bearing human melanoma cells.
AUTHOR: Hanada Takeshi; Toshinai Koji; Kajimura Naoko; Nara-Ashizawa Noriko; Tsukada Toshihiko; Hayashi Yujiro; Osuye Kazuhiro; Kangawa Kenji; Matsukura Shigeru; Nakazato

Masamitsu
CORPORATE SOURCE: Third Department of Internal Medicine, Miyazaki Medical College, Miyazaki 889-1692, Japan.
SOURCE: Biochemical and biophysical research communications, (2003 Feb 7) Vol. 301, No. 2, pp. 275-9. Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 5 Feb 2003
Last Updated on STN: 17 Apr 2003
Entered Medline: 15 Apr 2003

ABSTRACT:
Ghrelin is a novel brain-gut peptide that stimulates food intake and body weight gain. We studied the anabolic effect of ghrelin in a cancer cachexia mouse model. SEKI, a human melanoma cell line, was inoculated into nude mice to examine the effects of ghrelin on food intake and body weight. The intraperitoneal administration of ghrelin twice a day (6 nmol/mice/day) for 6 days suppressed weight loss in SEKI-inoculated mice and increased the rate of weight gain in vehicle-treated nude mice. ***Ghrelin*** administration also increased food intake in both SEKI- and vehicle-treated mice. Both the weight of white adipose tissue and the plasma leptin concentration were reduced in tumor-inoculated mice compared with vehicle-treated mice; these factors increased following ghrelin administration. The levels of both ghrelin peptide and mRNA in the stomach were upregulated in tumor-inoculated mice. The anabolic effect of ***ghrelin*** efficiently reverses the cachexia in mice bearing SEKI human melanoma. Ghrelin therefore may have a therapeutic ability to ameliorate cancer cachexia.

CONTROLLED TERM:
Check Tags: Female
Animals
Body Weight
*Cachexia
Cell Transplantation
Growth Inhibitors: BL, blood
Humans
Injections, Intraperitoneal
*Interleukin-6
Leptin: BL, blood
Leukemia Inhibitory Factor
Lymphokines: BL, blood
*Melanoma: ME, metabolism
Mice
Mice, Inbred BALB C
Mice, Nude
Neoplasms: PP, physiopathology
Peptide Hormones: AD, administration & dosage
*Peptide Hormones: ME, metabolism
Stomach: ME, metabolism
Tumor Cells, Cultured

CHEMICAL NAME: 0 (Growth Inhibitors); 0 (Interleukin-6); 0 (LIF protein, human); 0 (Leptin); 0 (Leukemia Inhibitory Factor); 0 (Lif protein, mouse); 0 (Lymphokines); 0 (Peptide Hormones); 0 (ghrelin)

L99 ANSWER 20 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2002619389 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12376579
TITLE: Hypophysectomy prevents ghrelin-induced adiposity and increases gastric ghrelin secretion in rats.
AUTHOR: Tschop Matthias; Flora David B; Mayer John P; Heiman Mark L
CORPORATE SOURCE: German Institute of Human Nutrition, Bergh.-Rehbrucke, Germany.. tschoep@mail.dife.de
SOURCE: Obesity research, (2002 Oct) Vol. 10, No. 10, pp. 991-9. Journal code: 9305691. ISSN: 1071-7323.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 12 Oct 2002
Last Updated on STN: 22 Jan 2003
Entered Medline: 21 Jan 2003

ABSTRACT:
OBJECTIVE: The novel gastric hormone ghrelin has recently been identified as an important modulator of energy homeostasis. Leptin-responsive hypothalamic neuropeptide Y/Agouti-related protein neurons are believed to mediate afferent ghrelin signals. Little is known, however, about ghrelin-induced efferent signals. We therefore investigated if hypothalamic-pituitary axes have a role in transferring ghrelin-induced changes of energy balance to the periphery. RESEARCH METHODS AND PROCEDURES: We subcutaneously injected hypophysectomized, as well as adrenalectomized, thyroidectomized, and sham-operated control rats with GH secretagogues [ghrelin, growth hormone (GH)-releasing peptide] for 1 week. Body weight, food intake, and body composition (chemical carcass analysis) were analyzed and compared with vehicle-treated controls. In addition, we quantified circulating levels of endogenous ghrelin in hypophysectomized and GH-treated normal rats. RESULTS: GH-secretagogue treatment of sham-operated control rats dose-proportionally increased food intake, body weight, and fat mass compared with vehicle-injected controls ($p < 0.01$). These effects, however, were not observed in ghrelin-treated hypophysectomized, thyroidectomized, or adrenalectomized rats, indicating an essential role for the pituitary axis in ghrelin-induced adiposity. Circulating levels of endogenous ghrelin were reduced by administration of GH in normal rats and were about 3-fold higher in hypophysectomized rats ($n = 20$, $p = 0.001$), suggesting a regulatory feedback loop involving the stomach and the pituitary to regulate gastric ghrelin secretion. DISCUSSION: According to these results, the endocrine pituitary is mediating ghrelin-induced changes toward a positive energy balance and is involved in the regulation of ghrelin secretion through a gastro-hypophyseal feedback loop.

CONTROLLED TERM: Check Tags: Male
Adipose Tissue: ME, metabolism
*Adipose Tissue: PH, physiology
Adrenalectomy
Animals
Body Weight: DE, drug effects
*Body Weight: PH, physiology
Eating: DE, drug effects
Eating: PH, physiology
Growth Hormone: ME, metabolism
Growth Hormone: PD, pharmacology
Hypophysectomy
Hypothalamo-Hypophyseal System: DE, drug effects
Hypothalamo-Hypophyseal System: ME, metabolism
*Hypothalamo-Hypophyseal System: PH, physiology
Insulin-Like Growth Factor I: PD, pharmacology
Oligopeptides: PD, pharmacology

Peptide Hormones: BL, blood
Peptide Hormones: ME, metabolism
*Peptide Hormones: PD, pharmacology
*Peptide Hormones: SE, secretion
Pituitary-Adrenal System: DE, drug effects
Pituitary-Adrenal System: ME, metabolism
*Pituitary-Adrenal System: PH, physiology
Rats
Rats, Sprague-Dawley
Thyroidectomy
CAS REGISTRY NO.: 67763-96-6 (Insulin-Like Growth Factor I); 87616-84-0 (growth hormone releasing hexapeptide); 9002-72-6 (Growth Hormone)
CHEMICAL NAME: 0 (Oligopeptides); 0 (Peptide Hormones); 0 (ghrelin); 0 (growth hormone-releasing peptide-2)

L99 ANSWER 21 OF 66 MEDLINE on STN
ACCESSION NUMBER: 2001643003 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11679419
TITLE: Chronic central infusion of ghrelin increases hypothalamic neuropeptide Y and Agouti-related protein mRNA levels and body weight in rats.
AUTHOR: Kamegai J; Tamura H; Shimizu T; Ishii S; Sugihara H; Wakabayashi I
CORPORATE SOURCE: Department of Medicine, Nippon Medical School, Tokyo, Japan.. jkamegai@nms.ac.jp
SOURCE: Diabetes, (2001 Nov) Vol. 50, No. 11, pp. 2438-43. Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 7 Nov 2001
Last Updated on STN: 23 Jan 2002
Entered Medline: 7 Dec 2001

ABSTRACT:
Ghrelin, an endogenous ligand for the growth hormone secretagogue receptor (GHS-R), was originally purified from the rat stomach. Like the synthetic growth hormone secretagogues (GHSs), ghrelin specifically releases growth hormone (GH) after intravenous administration. Also consistent with the central actions of GHSs, ghrelin-immunoreactive cells were shown to be located in the hypothalamic arcuate nucleus as well as the stomach. Recently, we showed that a single central administration of ghrelin increased food intake and hypothalamic agouti-related protein (AGRP) gene expression in rodents, and the orexigenic effect of this peptide seems to be independent of its GH-releasing activity. However, the effect of chronic infusion of ghrelin on food consumption and body weight and their possible mechanisms have not been elucidated. In this study, we determined the effects of chronic intracerebroventricular treatment with ghrelin on metabolic factors and on neuropeptide genes that are expressed in hypothalamic neurons that have been previously shown to express the GHS-R and to regulate food consumption. Chronic central administration of rat ghrelin (1 microg/rat every 12 h for 72 h) significantly increased food intake and body weight. However, it did not affect plasma insulin, glucose, leptin, or GH concentrations. We also found that chronic central administration of ghrelin increased both neuropeptide Y (NPY) mRNA levels (151.0 +/- 10.1% of saline-treated controls; $P < 0.05$) and AGRP mRNA levels (160.0 +/- 22.5% of saline-treated controls; $P < 0.05$) in the arcuate nucleus. Thus, the primary hypothalamic targets of ghrelin are

NPY/AGRP-containing neurons, and ghrelin is a newly discovered orexigenic peptide in the brain and stomach.

CONTROLLED TERM: Check Tags: Male
Animals
*Body Weight: DE, drug effects
Drug Administration Schedule
Eating: DE, drug effects
Gene Expression: DE, drug effects
Hypothalamus: DE, drug effects
*Hypothalamus: ME, metabolism
Injections, Intraventricular
Intercellular Signaling Peptides and Proteins
*Neuropeptide Y: ME, metabolism
*Peptide Hormones
*Peptides: AD, administration & dosage
Peptides: PD, pharmacology
*Proteins: GE, genetics
*RNA, Messenger: ME, metabolism
Rats
Rats, Sprague-Dawley

CHEMICAL NAME: 0 (Intercellular Signaling Peptides and Proteins); 0 (Neuropeptide Y); 0 (Peptide Hormones); 0 (Peptides); 0 (Proteins); 0 (RNA, Messenger); 0 (agouti-related protein); 0 (ghrelin)

L99 ANSWER 22 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2006:1357979 CAPLUS Full-text
DOCUMENT NUMBER: 146:99557
TITLE: Compositions and methods for modulating body weight and treating obesity-related disorders by gut hormone regulation.
INVENTOR(S): Meguid, Michael M.; Suzuki, Susumu
PATENT ASSIGNEE(S): The Research Foundation of State University of New York, USA
SOURCE: U.S. Pat. Appl. Publ., 17pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006293233	A1	20061228	US 2006-347195	20060203

PRIORITY APPLN. INFO.: US 2005-650003P P 20050204

AB The present invention relates to compns. and methods for regulating body weight, and for treating conditions associated with obesity, particularly obesity-related diabetes. The present invention is premised on the discovery that body weight can be effectively regulated by modulating the levels and/or activities of two gut hormones, PYY and ghrelin.

INCL 514012000
CC 17-6 (Food and Feed Chemistry)
Section cross-reference(s): 18, 63
IT Antidiabetic agents
Antiobesity agents
Appetite stimulants
Food additives

(compns. and methods for modulating body weight and treating obesity-related disorders by gut hormone regulation)
IT Appetite
(control of; compns. and methods for modulating body weight and treating obesity-related disorders by gut hormone regulation)
IT 106388-42-5, PYY 106388-42-5D, PYY, analogs 118997-30-1D, Human Peptide YY, amino acid sequence 3-36 246146-55-4, BIIE 0246 304853-26-7, Ghrelin 304853-26-7D, Ghrelin, analogs
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for modulating body weight and treating obesity-related disorders by gut hormone regulation)

L99 ANSWER 23 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2004:252369 CAPLUS Full-text
DOCUMENT NUMBER: 140:269531
TITLE: Autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss in human and animal
INVENTOR(S): Boving, Tine Elisabeth Gottschalk; Klysner, Steen
PATENT ASSIGNEE(S): Pharmexa A/s, Den.
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004024183	A1	20040325	WO 2003-DK592	20030912
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2498739	A1	20040325	CA 2003-2498739	20030912
AU 2003263150	A1	20040430	AU 2003-263150	20030912
EP 1539232	A1	20050615	EP 2003-794825	20030912
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1694724	A	20051109	CN 2003-825086	20030912
JP 2006504413	T	20060209	JP 2004-535024	20030912
MX 2005PA02699	A	20050920	MX 2005-PA2699	20050310
IN 2005KN00485	A	20060623	IN 2005-KN485	20050323
NO 2005001779	A	20050411	NO 2005-1779	20050411
ZA 2005002929	A	20060222	ZA 2005-2929	20050411

PRIORITY APPLN. INFO.: DK 2002-1345 A 20020912
US 2002-410164P P 20020912
WO 2003-DK592 W 20030912

AB Disclosed are novel methods that generally rely on immunization against autologous ghrelin. Immunization is preferably effected by administration of analogs of autologous ghrelin, said analogs being capable of inducing antibody production against the autologous ghrelin polypeptides. Especially preferred

as an immunogen is autologous ghrelin, which has been modified by introduction of one single or a few foreign, immunodominant and promiscuous T-cell epitopes. Also disclosed are nucleic acid vaccination against ghrelin and vaccination using live vaccines as well as methods and means useful for the vaccination. Such methods and means include methods for the preparation of analogs and pharmaceutical formulations, as well as nucleic acid fragments, vectors, transformed cells, polypeptides and pharmaceutical formulations.

IC ICM A61K039-39
ICS A61K039-385; A61K039-00; C07K014-435; A61P003-04

CC 15-2 (Immunochemistry)
Section cross-reference(s): 3, 63

IT Amide group
Animal cell
Animal cell line
Animals
Anorexia
Antigen presentation
Antigen-presenting cell
Bos taurus
Burn
Cachexia
Canis familiaris
DNA sequences
Epitopes
Eubacteria
Eukaryota
Fungi
Genetic vectors
Human
Immunostimulants
Immunotherapy
Influenza virus
Microorganism
Molecular cloning
Mus
Obesity
PCR (polymerase chain reaction)
Plant cell
Plasmodium falciparum
Prokaryota
Protein sequences
Protozoa
Rattus
Sterculia urens
Sus scrofa domestica
Viral vectors
Wound
Yeast
cDNA sequences
(autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

IT Body weight
(excess gain; autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

IT Body weight
(loss; autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

IT 126779-13-3P 126779-14-4P 161147-59-7P 304853-26-7DP,
Ghrelin, epitopic and chimeric derivs. 674383-81-4P 674383-82-5P
674383-83-6P 674383-84-7P 674383-85-8P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 24 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 2004:80708 CAPLUS Full-text
DOCUMENT NUMBER: 140:140069
TITLE: Synthesis and therapeutic uses of ghrelin analogs
INVENTOR(S): Dong, Zheng Xin; Shen, Yeelana
PATENT ASSIGNEE(S): Scientifiques (S.C.R.A.S.) Societe De Conseils De Recherches Et D'Application, Fr.
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009616	A2	20040129	WO 2003-US22925	20030723
WO 2004009616	A3	20060209		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2491946	A1	20040129	CA 2003-2491946	20030723
AU 2003254119	A1	20040209	AU 2003-254119	20030723
EP 1578778	A2	20050928	EP 2003-765930	20030723
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006515271	T	20060525	JP 2004-523304	20030723
CN 1832753	A	20060913	CN 2003-817446	20030723
BR 2003012871	A	20070710	BR 2003-12871	20030723
NO 2005000083	A	20050323	NO 2005-83	20050106
MX 2005PA00908	A	20050722	MX 2005-PA908	20050121
US 2005272648	A1	20051208	US 2005-522398	20050121
IN 2005KN00153	A	20060609	IN 2005-KN153	20050208

PRIORITY APPLN. INFO.:
US 2002-397834P P 20020723
US 2002-427488P P 20021119
WO 2003-US22925 W 20030723

AB The invention comprises the synthesis of peptidyl ghrelin analogs that possess agonist or antagonist activity toward growth hormone secretagogue receptor, along with therapeutic and non-therapeutic uses thereof.

IC ICM C07K

CC 2-10 (Mammalian Hormones)

Section cross-reference(s): 34
IT AIDS (disease)
Anorexia
Bulimia
Cachexia
Chemotherapy
Dialysis
Immobilization, animal
Radiotherapy
(-associated weight loss; synthesis and therapeutic uses of ghrelin analogs)
IT Cachexia
(cancerous, -associated weight loss; synthesis and therapeutic uses of ghrelin analogs)
IT Calculi, biliary
Hypertension
Neoplasm
Osteoarthritis
(excessive weight contributing to; synthesis and therapeutic uses of ghrelin analogs)
IT Body weight
(gain and maintenance; synthesis and therapeutic uses of ghrelin analogs)
IT Body weight
(loss, accessory to another disorder; synthesis and therapeutic uses of ghrelin analogs)
IT Antiarthritics
Antidiabetic agents
Antihypertensives
Antiobesity agents
Appetite
Appetite depressants
Appetite stimulants
Cardiovascular agents
Cardiovascular system, disease
Diabetes mellitus
Drug delivery systems
Human
Obesity
Sexual disorders
Wound
Wound healing
Wound healing promoters
(synthesis and therapeutic uses of ghrelin analogs)
IT Disease, animal
(wasting, -associated weight loss; synthesis and therapeutic uses of ghrelin analogs)
IT 304853-26-7DP, Ghrelin, analogs 651048-33-8P 651048-34-9P
651048-35-0P 651048-36-1P 651048-37-2P 651048-38-3P 651048-39-4P
651048-40-7P 651048-41-8P 651048-42-9P 651048-43-0P 651048-44-1P
651048-45-2P 651048-46-3P 651048-47-4P 651048-48-5P 651048-49-6P
651048-50-9P 651048-51-0P 651048-52-1P 651048-53-2P 651048-54-3P
651048-55-4P 651048-56-5P 651048-57-6P 651048-58-7P 651048-59-8P
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651048-70-3P 651048-71-4P 651048-72-5P 651048-73-6P 651048-74-7P
651048-75-8P 651048-76-9P 651048-77-0P 651048-78-1P 651048-79-2P
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651048-85-0P 651048-86-1P 651048-87-2P 651048-88-3P 651048-89-4P
651048-90-7P 651048-91-8P 651048-92-9P 651048-93-0P 651048-94-1P

651048-95-2P 651048-96-3P 651048-97-4P 651048-98-5P 651048-99-6P
651049-00-2P 651049-01-3P 651049-02-4P 651049-03-5P 651049-04-6P
651049-05-7P 651049-08-0P 651049-10-4P 651049-12-6P 651049-13-7P
651049-14-8P 651049-16-0P 651049-17-1P 651049-18-2P 651049-19-3P
651049-20-6P 651049-21-7P 651049-22-8P 651049-23-9P 651049-24-0P
651049-25-1P 651049-26-2P 651049-27-3P 651049-28-4P 651049-29-5P
651049-30-8P 651049-31-9P 651049-32-0P 651049-33-1P 651049-34-2P
651049-35-3P 651049-36-4P 651049-37-5P 651049-38-6P 651049-39-7P
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651049-56-8P 651049-57-9P 651049-58-0P 651049-59-1P 651049-60-4P
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651049-66-0P 651049-67-1P 651049-68-2P 651049-69-3P 651049-70-6P
651049-71-7P 651049-72-8P 651049-73-9P 651049-74-0P 651049-75-1P
651049-76-2P 651049-77-3P 651049-78-4P 651049-79-5P 651049-80-8P
651049-81-9P 651049-82-0P 651049-83-1P 651049-84-2P 651049-85-3P
651049-86-4P 651049-87-5P 651049-88-6P 651049-89-7P 651049-90-0P
651049-91-1P 651049-92-2P 651049-93-3P 651049-94-4P 651049-95-5P
651049-96-6P 651049-97-7P 651049-98-8P 651049-99-9P 651050-00-9P
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651050-11-2P 651050-12-3P 651050-13-4P 651050-14-5P 651050-15-6P
651050-16-7P 651050-17-8P 651050-18-9P 651050-19-0P 651050-20-3P
651050-21-4P 651050-22-5P 651050-23-6P 651050-24-7P 651050-25-8P
651050-26-9P 651050-27-0P 651050-28-1P 651050-29-2P 651050-30-5P
651050-31-6P 651050-32-7P 651050-33-8P 651050-34-9P 651050-35-0P
651050-36-1P 651050-37-2P 651050-38-3P 651050-39-4P 651050-40-7P
651050-41-8P 651050-42-9P 651050-43-0P 651050-44-1P 651050-45-2P
651050-46-3P 651050-47-4P 651050-48-5P 651050-49-6P 651050-50-9P
651050-51-0P 651050-52-1P 651050-53-2P 651050-54-3P 651050-55-4P
651050-56-5P 651050-57-6P 651050-58-7P 651050-59-8P 651050-60-1P
651050-61-2P 651050-62-3P 651050-63-4P 651050-64-5P 651050-65-6P
651050-66-7P 651050-67-8P 651050-68-9P 651050-69-0P 651050-70-3P
651050-71-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and therapeutic uses of ghrelin analogs)

L99 ANSWER 25 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 2005:39282 CAPLUS Full-text
DOCUMENT NUMBER: 142:233614
TITLE: Novel ghrelin analogs with improved affinity for the GH secretagogue receptor stimulate GH and prolactin release from human pituitary cells
AUTHOR(S): Rubinfeld, H.; Hadani, M.; Taylor, J. E.; Dong, J. Z.; Comstock, J.; Shen, Y.; DeOliveira, D.; Datta, R.; Culler, M. D.; Shimon, I.
CORPORATE SOURCE: Institute of Endocrinology, Chaim Sheba Medical Center, Tel-Hashomer, 52621, Israel
SOURCE: European Journal of Endocrinology (2004), 151(6), 787-795
CODEN: EJOEEP; ISSN: 0804-4643
PUBLISHER: BioScientifica Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ghrelin, a recently identified 28-amino acid peptide is a potent GH secretagogue (GHS) produced predominantly by the stomach. Ghrelin stimulates GH secretion through binding to the GHS receptor in the hypothalamus and

pituitary. In addition to the GH-releasing action, ghrelin has been found to be a powerful orexigenic factor. To assess the direct in vitro effects of ghrelin on human pituitary hormone secretion the authors have produced a panel of novel ghrelin analogs (mol. weight, 3323-3384; human native ghrelin, 3371) with enhanced affinity for the human GHS receptor (IC50 0.38-1.09 nM; human ghrelin, 1.2-2.2 nM). The peptidic analogs were tested for their effect on GH secretion using dispersed human fetal pituitaries (21 to 23 wk of gestation) and cultured GH- and prolactin (PRL)-secreting adenomas. The expression of the GHS receptor in normal (fetal and adult) human pituitary tissues, GH- and PRL-cell adenomas was established using RT-PCR. The effects of ghrelin, its analogs and GH-releasing hormone (GHRH) alone or in combination on GH and PRL secretion were compared at various concns. The ghrelin analogs stimulated GH release by 35-60% from human fetal pituitary cells (1-10 nM) and by 50-75% from cultured pituitary adenomas (10 nM). This releasing effect was dose-dependent, achieving maximal stimulation with analog concns. at 100 nM. Human ghrelin was less potent as compared with its analogs in stimulating human GH, in keeping with the improved binding affinity of the analogs for the GHS-1a receptor. The ghrelin analogs and GHRH had comparable effects on GH secretion from both normal and adenomatous cells, and in combination produced an additive stimulatory effect on GH (150%). In contrast, ghrelin and its analogs induced a comparable increase in PRL release ranging between 25 and 40% from fetal cells and 30 and 70% from cultured PRL-cell and mixed GH-PRL adenomas. The authors' results have demonstrated for the first time that ghrelin analogs with enhanced affinity for the GHS receptor are potent stimulators of GH secretion from human pituitary cells, and thus may possess potential clin. therapeutic benefits.

CC 2-6 (Mammalian Hormones)

IT Pituitary gland, anterior lobe, neoplasm
(adenoma; ghrelin analogs with improved affinity for GH secretagogue receptor stimulation of GH and prolactin release from human pituitary cells)

IT 258279-04-8, Human ghrelin 304853-26-7D, Ghrelin, analogs
844819-35-8, BIM 28125 844819-36-9, BIM 28143 844819-37-0, BIM 28152
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ghrelin analogs with improved affinity for GH secretagogue receptor stimulation of GH and prolactin release from human pituitary cells)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 26 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:998603 CAPLUS Full-text
TITLE: Human anti-human acyl-ghrelin antibodies and binding members for treating ghrelin related disease including obesity
INVENTOR(S): Edwards, Bryan Michael; Welsh, Fraser Ewing; Boyle, Melanie; Lane, Steven Godfrey; Bland-Ward, Philip Antony; Sleeman, Matthew Alexander
PATENT ASSIGNEE(S): Cambridge Antibody Technology Limited, UK
SOURCE: PCT Int. Appl., 94pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007099346	A1	20070907	WO 2007-GB741	20070305

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-779263P P 20060303

AB This invention relates to binding members for ghrelin, in particular anti-acyl ghrelin antibody mols., especially human antibody mols. comprising the sequences set out herein, and especially those that neutralize acyl-ghrelin activity. Anti-ghrelin antibody mols. of the invention may be used in the diagnosis or treatment of ghrelin-related disorders, including obesity.

CC 15-3 (Immunochemistry)
Section cross-reference(s): 3, 63

IT INDEXING IN PROGRESS

IT Appetite
(satiety, impairment; human anti-human acyl-ghrelin antibodies and binding members for treating ghrelin related disease including obesity)

IT Appetite
(suppression; human anti-human acyl-ghrelin antibodies and binding members for treating ghrelin related disease including obesity)

IT 304853-26-7D, Ghrelin, acyl derivative
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(human anti-human acyl-ghrelin antibodies and binding members for treating ghrelin related disease including obesity)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 27 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:969819 CAPLUS Full-text
TITLE: Cell-targeted IκB and methods for the use thereof
INVENTOR(S): Liu, Yuying; Rosenblum, Michael G.
PATENT ASSIGNEE(S): Research Development Foundation, USA
SOURCE: U.S. Pat. Appl. Publ., 35pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007202593	A1	20070830	US 2007-679630	20070227
WO 2007101202	A1	20070907	WO 2007-US62887	20070227

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,

CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-777016P P 20060227

AB Activation of nuclear factor κB (NF-κB) is involved in a number of diseases such as viral and bacterial infections, and cell proliferative disorders such as cancer and autoimmune disease. In certain instances, constitutive NF-κB activity has also been liked to the resistance of certain cancers to chemo and radiation therapy. The instant invention concerns method of inhibiting NF-κB activity in target cell populations by deliver of a polypeptide inhibitor of NF-κB (IκB). Methods of the invention may be used to treat diseases such as infections, and cell proliferative disorders. Methods for sensitizing cells to apoptosis and cytotoxic therapies are also described.

INCL 435325000; 435235100

CC 1-12 (Pharmacology)

IT INDEXING IN PROGRESS

IT Antitumor agents
Autoimmune disease
Bladder, neoplasm
Bone, neoplasm
Brain, neoplasm
Chemosensitizers, pharmaceutical
Cytotoxic agents
Esophagus, neoplasm
Gene therapy
Head and Neck, neoplasm
Human
Immunotherapy
Kidney, neoplasm
Leukemia
Liver, neoplasm
Lung, neoplasm
Mammary gland, neoplasm
Melanoma
Neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Prostate gland, neoplasm
Radiosensitizers, biological
Radiotherapy
Skin, neoplasm
Spleen, neoplasm
Testis, neoplasm
(cell-targeted IκB for inhibition of NF-κB and treatment of diseases and combination with other agents)

IT Uterus, neoplasm
(cervix; cell-targeted IκB for inhibition of NF-κB and treatment of diseases and combination with other agents)

IT Intestine, neoplasm
(colon; cell-targeted IκB for inhibition of NF-κB and treatment of diseases and combination with other agents)

IT Neoplasm, neoplasm
(head and neck; cell-targeted IκB for inhibition of NF-κB and treatment of diseases and combination with other agents)

IT 50-14-6D, Calciferol, conjugates with IκB 50-56-6D, Oxytocin, conjugates with IκB 51-21-8, 5-Fluorouracil 51-41-2D, Noradrenaline, conjugates with IκB 51-43-4D, Adrenaline, conjugates with IκB 51-48-9D, Thyroxine, conjugates with IκB

51-61-6D, Dopamine, conjugates with IκB 57-22-7, Vincristine 57-83-0D, Progesterone, conjugates with IκB 73-31-4D, Melatonin, conjugates with IκB 1393-25-5D, Secretin, conjugates with IκB 7689-03-4, Camptothecin 9002-60-2D, Adrenocorticotropic hormone, conjugates with IκB 9002-61-3D, Human chorionic gonadotropin, conjugates with IκB 9002-62-4D, Prolactin, conjugates with IκB 9002-64-6D, Parathyroid hormone, conjugates with IκB 9002-67-9D, Luteinizing hormone, conjugates with IκB 9002-68-0D, Follicle-stimulating hormone, conjugates with IκB 9002-71-5D, Thyroid-stimulating hormone, conjugates with IκB 9002-72-6D, Growth hormone, conjugates with IκB 9002-76-0D, Gastrin, conjugates with IκB 9004-10-8D, Insulin, conjugates with IκB 9007-12-9D, Calcitonin, conjugates with IκB 9007-92-5D, Glucagon, conjugates with IκB 9011-97-6D, Cholecystokinin, conjugates with IκB 9014-42-0D, Thrombopoietin, conjugates with IκB 9015-71-8D, Corticotropin-releasing hormone, conjugates with IκB 9034-39-3D, Growth hormone releasing hormone, conjugates with IκB 9034-40-6D, LH-RH, conjugates with IκB 9083-38-9D, MIF, conjugates with IB 11000-17-2D, Antidiuretic hormone, conjugates with IκB 11002-13-4D, Angiotensinogen, conjugates with IκB 11096-26-7D, Erythropoietin, conjugates with IκB 15663-27-1, Cisplatin 23214-92-8, Doxorubicin 24305-27-9D, Thyrotropin-releasing hormone, conjugates with IκB 32222-06-3D, Calcitriol, conjugates with IκB 33069-62-4, Paclitaxel 33419-42-0, Etoposide 51110-01-1D, Somatostatin, conjugates with IκB 61912-98-9D, Insulin-like growth factor, conjugates with IκB 62031-54-3D, Fibroblast growth factor, conjugates with IκB 62229-50-9D, Epidermal growth factor, conjugates with IκB 67763-96-6D, insulin-like growth factor-1, conjugates with IκB 81627-83-0D, Macrophage-colony stimulating factor, conjugates with IκB 82785-45-3D, Neuropeptide Y, conjugates with IκB 83869-56-1D, Granulocyte-macrophage colony stimulating factor, conjugates with IκB 85637-73-6D, Atrial natriuretic peptide, conjugates with IκB 95058-81-4, Gemcitabine 106602-62-4D, Amylin, conjugates with IκB 106956-32-5D, Oncostatin M, conjugates with IκB 126339-09-1D, Peptide YY(3-36), conjugates with IκB 127464-60-2D, Vascular endothelial growth factor, conjugates with IκB 143011-72-7D, Granulocyte-colony stimulating factor, conjugates with IκB 169494-85-3D, Leptin, conjugates with IκB 179324-69-7, Velcade 304853-26-7D, Ghrelin, conjugates with IκB

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cell-targeted IκB for inhibition of NF-κB and treatment of diseases and combination with other agents)

L99 ANSWER 28 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:230501 CAPLUS Full-text

DOCUMENT NUMBER: 146:258657

TITLE: Fusion products of human serum albumin and therapeutic proteins for use in the treatment of disease

INVENTOR(S): Rosen, Craig A.; Haseltine, William A.; Moore, Paul A.; Bock, Jason B.; Bell, Adam; Shi, Yanggu; Lafleur, David W.

PATENT ASSIGNEE(S): Human Genome Sciences, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 182pp., Cont.-in-part of Appl. No. PCT/US2005/004041.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007048282	A1	20070301	US 2006-500314	20060808
WO 2005077042	A2	20050825	WO 2005-US4041	20050209
WO 2005077042	A3	20061130		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2004-542274P P 20040209
US 2004-549901P P 20040305
US 2004-556906P P 20040329
US 2004-636603P P 20041217
WO 2005-US4041 A2 20050209

AB Fusion products of human serum albumin with therapeutic proteins are described for use in the treatment and prevention of disease. Chimeric genes encoding these proteins are described for use in manufacture of the fusion protein. Preparation and use of fusion proteins of human serum albumin and brain natriuretic peptide is demonstrated.

INCL 424085700; 514012000; 530350000; 530351000; 530363000; 435069510; 435069700; 435320100; 435325000
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 3
IT Bone, disease
Cardiovascular system, disease
Growth disorders, animal
Immune disease
Kidney, disease
Metabolic disorders
Muscle, disease
Neoplasm
Neurotoxicity
Pain
(treatment of; fusion products of human serum albumin and therapeutic proteins for use in treatment of disease)
IT 9001-08-5DP, Butyrylcholinesterase, fusion products with human serum albumin 9001-67-6DP, Neuraminidase, fusion products with human serum albumin 9002-12-4DP, Uricase, fusion products with human serum albumin 9002-72-6DP, Somatotropin, fusion products with human serum albumin 9027-98-9DP, fusion products with human serum albumin 37228-64-1DP, fusion products with human serum albumin 62340-29-8DP, Oxyntomodulin, fusion products with human serum albumin 67763-96-6DP, IGF-1, fusion products with human serum albumin 83652-28-2DP, Calcitonin gene-related peptide, fusion products with human serum albumin 85637-73-6DP, Atrial natriuretic peptide, fusion products with human serum albumin

89750-14-1DP, Glucagon-like peptide I, fusion products with human serum albumin 106388-42-5DP, Peptide YY, fusion products with human serum albumin 116243-73-3DP, Endothelin, fusion products with human serum albumin 127830-04-0DP, C-Type natriuretic peptide, fusion products with human serum albumin 143863-92-7DP, Dendroaspis natriuretic peptide, fusion products with human serum albumin 154835-90-2DP, Adrenomedullin, fusion products with human serum albumin 165724-54-9DP, Long-acting natriuretic peptide, fusion products with human serum albumin 171714-28-6DP, 31-67-γ-Atrial natriuretic peptide, fusion products with human serum albumin 186207-03-4DP, TIMP-4, fusion products with human serum albumin 201615-39-6DP, Kaliuretic peptide, fusion products with human serum albumin 304853-26-7DP, Ghrelin, fusion products with human serum albumin 388138-21-4DP, Metastin, fusion products with human serum albumin 426206-97-5DP, β-Defensin 2, fusion products with human serum albumin
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fusion products of human serum albumin and therapeutic proteins for use in treatment of disease)

L99 ANSWER 29 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:175512 CAPLUS Full-text
DOCUMENT NUMBER: 146:229617
TITLE: Preparation of tryptophan-derived triazole derivatives as ghrelin analogue ligands of growth hormone secretagogue receptors
INVENTOR(S): Perrissoud, Daniel; Martinez, Jean; Moulin, Aline; Fehrentz, Jean-Alain; Boeglin, Damien; Demange, Luc
PATENT ASSIGNEE(S): Zentaris GmbH, Germany; Le Centre National de la Recherche Scientifique; University of Montpellier I; University of Montpellier II
SOURCE: U.S. Pat. Appl. Publ., 123 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007037857	A1	20070215	US 2006-502473	20060811
US 2007208061	A2	20070906		
EP 1757290	A1	20070228	EP 2005-17732	20050816

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

PRIORITY APPLN. INFO.:
US 2005-707941P P 20050815
EP 2005-17732 A 20050816
US 2006-787543P P 20060331

OTHER SOURCE(S): MARPAT 146:229617

AB The invention provides novel triazole derivs. I [R1, R2 are H, (cyclo)alkyl, (hetero)aryl, heterocyclyl, sulfonyl, etc.; one of R3 and R4 is H and the other is (cyclo)alkyl, (hetero)aryl, heterocyclyl, sulfonyl, etc.; R5 is (cyclo)alkyl, (hetero)aryl, sulfonyl, acyl, etc.; R6 is H, (cyclo)alkyl, or cycloalkylalkyl; n is 0-2] as ghrelin analog ligands of growth hormone secretagogue receptors that are useful in the treatment or prophylaxis of physiol. and/or pathophysiol. conditions in mammals, preferably humans, that are mediated by GHS receptors. The invention further provides GHS receptor antagonists and agonists that can be used for modulation of these receptors and are useful for treating conditions such as growth retardation, cachexia,

short-, medium- and/or long term regulation of energy balance or food intake, adipogenesis, adiposity and/or obesity, body weight gain and/or reduction, diabetes, tumor cell proliferation, inflammation, postoperative ileus and/or gastrectomy (ghrelin replacement therapy). Thus, compound II was prepared by reactions of Boc-protected D-tryptophan, 2,4-dimethoxybenzylamine, 3-(1H-indol-3- yl)propanoic hydrazide, and Boc-2-amino-2-methylpropanoic acid. A figure shows biol. activity of II, i.e., the calculated dose-response plots of the in vitro intracellular calcium release assay with human GHS-R1a transfected CHO cells (GHS antagonist values IC50 = 1.42 x 10-6 and Kb = 1.23 x 10-8 M).

INCL 514341000; 514383000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 2, 28
IT Alzheimer's disease
Anorexia
Anti-Alzheimer's agents
Anti-inflammatory agents
Antidepressants
Antidiabetic agents
Antihypertensives
Antiobesity agents
Antitumor agents
Anxiety
Anxiolytics
Body weight
Cachexia
Cardiomyopathy
Central nervous system, disease
Cushing's syndrome
Energy balance
Feeding
Heart, disease
Heart failure
Homeostasis
Hunger
Hypertension
Hypothermia
Immunity
Immunodeficiency
Immunosuppression
Inflammation
Lipodystrophy
Lung, disease
Multiple sclerosis
Neoplasm
Obesity
Osteoporosis
Ovulation induction
Prader-Willi syndrome
Schizophrenia
Sleep disorders
Transplant and Transplantation
Turner syndrome
Wound healing
(preparation of tryptophan-derived triazole derivs. as ghrelin analog ligands of growth hormone secretagogue receptors)
IT Disease, animal
(wasting; preparation of tryptophan-derived triazole derivs. as ghrelin analog ligands of growth hormone secretagogue receptors)
IT 304853-26-7DP, Ghrelin, analogs 925238-36-4P 925238-37-5P

925238-38-6P 925238-39-7P 925238-40-0P 925238-41-1P 925238-42-2P
925238-43-3P 925238-44-4P 925238-45-5P 925238-46-6P 925238-47-7P
925238-48-8P 925238-49-9P 925238-50-2P 925238-51-3P 925238-52-4P
925238-53-5P 925238-54-6P 925238-55-7P 925238-56-8P 925238-57-9P
925238-58-0P 925238-59-1P 925238-60-4P 925238-61-5P 925238-62-6P
925238-63-7P 925238-64-8P 925238-65-9P 925238-66-0P 925238-67-1P
925238-69-3P 925238-71-7P 925238-73-9P 925238-75-1P 925238-77-3P
925238-78-4P 925238-79-5P 925238-80-8P 925238-81-9P 925238-82-0P
925238-83-1P 925238-84-2P 925238-85-3P 925238-86-4P 925238-87-5P
925238-88-6P 925238-89-7P 925238-90-0P 925238-91-1P 925238-92-2P
925238-93-3P 925238-94-4P 925238-95-5P 925238-96-6P 925238-97-7P
925238-98-8P 925238-99-9P 925239-00-5P 925239-01-6P 925239-02-7P
925239-03-8P 925239-04-9P 925239-05-0P 925239-06-1P 925239-07-2P
925239-08-3P 925239-09-4P 925239-10-7P 925239-11-8P 925239-12-9P
925239-13-0P 925239-14-1P 925239-15-2P 925239-16-3P 925239-17-4P
925239-18-5P 925239-19-6P 925239-20-9P 925239-21-0P 925239-22-1P
925239-23-2P 925239-24-3P 925239-25-4P 925239-26-5P 925239-27-6P
925239-28-7P 925239-29-8P 925239-30-1P 925239-31-2P 925239-32-3P
925239-33-4P 925239-34-5P 925239-35-6P 925239-36-7P 925239-37-8P
925239-38-9P 925239-39-0P 925239-40-3P 925239-41-4P 925239-42-5P
925239-43-6P 925239-44-7P 925239-45-8P 925239-46-9P 925239-47-0P
925239-48-1P 925239-49-2P 925239-50-5P 925239-51-6P 925239-52-7P
925239-53-8P 925239-54-9P 925239-55-0P 925239-56-1P 925239-57-2P
925239-58-3P 925239-59-4P 925239-60-7P 925239-61-8P 925239-62-9P
925239-63-0P 925239-64-1P 925239-65-2P 925239-66-3P 925239-67-4P
925239-68-5P 925239-69-6P 925239-70-9P 925239-71-0P 925239-72-1P
925239-73-2P 925239-74-3P 925239-75-4P 925239-76-5P 925239-77-6P
925239-78-7P 925239-79-8P 925239-80-1P 925239-81-2P 925239-82-3P
925239-83-4P 925239-84-5P 925239-85-6P 925239-86-7P 925239-87-8P
925239-88-9P 925239-89-0P 925239-90-3P 925239-91-4P 925239-92-5P
925239-93-6P 925239-94-7P 925239-95-8P 925239-96-9P 925239-97-0P
925239-98-1P 925239-99-2P 925240-00-2P 925240-01-3P 925240-02-4P
925240-03-5P 925240-04-6P 925240-05-7P 925240-06-8P 925240-07-9P
925240-08-0P 925240-09-1P 925240-10-4P 925240-11-5P 925240-12-6P
925240-13-7P 925240-14-8P 925240-15-9P 925240-16-0P 925240-17-1P
925240-18-2P 925240-19-3P 925240-20-6P 925240-21-7P 925240-22-8P
925240-23-9P 925240-24-0P 925240-25-1P 925240-26-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tryptophan-derived triazole derivs. as ghrelin analog ligands of growth hormone secretagogue receptors)

L99 ANSWER 30 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:746488 CAPLUS Full-text
DOCUMENT NUMBER: 147:269463
TITLE: Exercise-induced suppression of acylated ghrelin in humans
AUTHOR(S): Broom, D. R.; Stensel, D. J.; Bishop, N. C.; Burns, S. F.; Miyashita, M.
CORPORATE SOURCE: School of Sport and Exercise Sciences, Loughborough University, Leicestershire, UK
SOURCE: Journal of Applied Physiology (2007), 102(6), 2165-2171
CODEN: JAPHEV; ISSN: 8750-7587
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ghrelin is an orexigenic hormone secreted from endocrine cells in the stomach and other tissues. Acylation of ghrelin is essential for appetite regulation.

Vigorous exercise induces appetite suppression, but this does not appear to be related to suppressed concns. of total ghrelin. This study examined the effect of exercise and feeding on plasma acylated ghrelin and appetite. Nine male subjects aged 19-15 yr participated in two, 9-h trials (exercise and control) in a random crossover design. Trials began at 0800 in the morning after an overnight fast. In the exercise trial, subjects ran for 60 min at 72% of maximum oxygen uptake between 0800 and 0900. After this, they rested for 8 h and consumed a test meal at 1100. In the control trial, subjects rested for 9 h and consumed a test meal at 1100. Area under the curve values for plasma acylated ghrelin concentration (assessed from venous blood samples) were lower over the first 3 h and the full 9 h of the exercise trial compared with the control trial: 317 ± 135 vs. 510 ± 186 pg · ml-1 · 3 h and 917 ± 342 vs. 1,401 ± 521 pg · ml-1 · 9 h (means ± SE) resp. ($P < 0.05$). Area under the curve values for hunger (assessed using a visual scale) were lower over the first 3 h of the exercise trial compared with the control trial ($P = 0.013$). These findings demonstrate that plasma acylated ghrelin concentration and hunger are suppressed during running.

CC 2-6 (Mammalian Hormones)
Section cross-reference(s): 13
ST exercise acylated ghrelin appetite hunger
IT Appetite
(hunger was suppressed during and immediate after exercise in human)
IT 304853-26-7D, Ghrelin, acylated
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(plasma acylated ghrelin level was reduced during exercise in human)
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 31 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:261317 CAPLUS Full-text
DOCUMENT NUMBER: 146:435473
TITLE: Characterization of proghrelin peptides in mammalian tissue and plasma
AUTHOR(S): Bang, Angela S.; Soule, Steven G.; Yandle, Tim G.; Richards, A. Mark; Pemberton, Chris J.
CORPORATE SOURCE: Christchurch Cardioendocrine Research Group, Department of Medicine, University of Otago, Christchurch, 8140, N. Z.
SOURCE: Journal of Endocrinology (2007), 192(2), 313-323
CODEN: JOENAK; ISSN: 0022-0795
PUBLISHER: Society for Endocrinology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ghrelin is a 28 amino acid stomach peptide, derived from proghrelin(1-94), that stimulates GH release, appetite and adipose deposition. Recently, a peptide derived from proghrelin(53-75) - also known as obestatin - has been reported to be a physiol. antagonist of ghrelin in the rat. Using four specific RIAs, we provide the first characterization of proghrelin(1-94) peptides in human plasma, their modulation by metabolic manipulation and their distribution in mammalian tissues. Ghrelin(1-28) immunoreactivity (IR) in human plasma and rat plasma/stomach consisted of major des-octanoyl and minor octanoylated forms, as determined by HPLC/RIA. Human plasma ghrelin(1-28) IR was significantly suppressed by food intake, oral glucose and 1 mg s.c. glucagon administration. Ghrelin(1-28) IR and proghrelin(29-94) IR peptide distributions in the rat indicated that the stomach and gastrointestinal tract contain the highest amts. of the peptides. Human and rat plasma and rat stomach exts. contained a major IR peak of proghrelin(29-94)-like peptide as determined by HPLC/RIA, whereas no obestatin IR was observed Human plasma proghrelin(29-94)-like IR pos. correlated with ghrelin(1-28) IR, was significantly suppressed by food intake and oral glucose and shared with

ghrelin(1-28) IR a neg. correlation with body mass index. We found no evidence for the existence of obestatin as a unique, endogenous peptide. Rather, our data suggest that circulating and stored peptides derived from the carboxyl terminal of proghrelin (C-ghrelin) are consistent in length with proghrelin(29-94) and respond to metabolic manipulation, at least in man, in similar fashion to ghrelin(1-28).

CC 2-6 (Mammalian Hormones)
IT Body weight
(lean; characterization of mammalian plasma/tissue proghrelin peptides and influence of food intake, oral glucose and glucagon administration)
IT 9034-39-3, Somatoliberin 37221-79-7, VIP 51110-01-1, Somatostatin 52906-92-0, Motilin 82785-45-3, Neuropeptide Y 89750-14-1, GLP-1 111745-44-9, Neuromedin U 126339-09-1 245359-74-4, Orexin (peptide) 304853-26-7D, Ghrelin, desoctanoyl
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(characterization of mammalian plasma/tissue proghrelin peptides and its cross reactivity with other peptides and hormones)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 32 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:808457 CAPLUS Full-text
DOCUMENT NUMBER: 147:134801
TITLE: Variations in the preproghrelin gene correlate with higher body mass index, fat mass, and body dissatisfaction in young Japanese women
AUTHOR(S): Ando, Tetsuya; Ichimaru, Yuhei; Konjiki, Fujiko; Shoji, Masayasu; Komaki, Gen
CORPORATE SOURCE: Department of Psychosomatic Research, National Institute of Mental Health, National Center of Neurology and Psychiatry, Kodaira, Tokyo, Japan
SOURCE: American Journal of Clinical Nutrition (2007), 86(1), 25-32
CODEN: AJCNAC; ISSN: 0002-9165
PUBLISHER: American Society for Nutrition
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Ghrelin is an endogenous peptide that stimulates growth hormone secretion, enhances appetite, and increases body weight and may play a role in eating disorders. Objective: The purpose was to determine whether any preproghrelin gene variants are associated with anthropometric measures, circulating ghrelin, lipid concns., insulin resistance, or psychol. measures relevant to eating disorders in young women. Design: This cross-sectional study compared outcome measures between preproghrelin genotypes. The participants in the study included 264 Japanese women [university students with a mean (±SD) age of 20.4±0.7] with no history of eating disorders. The main outcomes were responses to the Eating Disorder Inventory-2 (EDI-2), anthropometric measures, measures of depression and anxiety, and fasting blood concns. of acylated or desacyl ghrelin, lipids, glucose, and insulin. Results: Two single nucleotide polymorphisms (SNPs) whose minor allele frequencies were >0.05-the Leu72Met (408C→A) SNP in exon 2 and the 3056 T→C SNP in intron 2-were used for association anal. The 3056C allele was significantly associated with a higher acylated ghrelin concentration ($P = 0.0021$), body weight ($P = 0.011$), body mass index ($P = 0.007$), fat mass ($P = 0.012$), waist circumference ($P = 0.008$), and skinfold thickness ($P = 0.011$) and a lower HDL-cholesterol concentration ($P = 0.02$). Interestingly, the 3056C allele was related to elevated scores in the Drive for Thinness-Body Dissatisfaction (DT-BD) subscale of the EDI-2 ($P = 0.003$). Conclusion: Our findings suggest that the preproghrelin gene 3056T→C SNP is associated with

changes in basal ghrelin concns. and phys. and psychol. variables related to eating disorders and obesity.

CC 2-6 (Mammalian Hormones)

IT Body weight
(lean; variations in preproghrelin gene correlated with insulin resistance, altered blood lipids, higher body mass index, fat mass, and body dissatisfaction in young Japanese women)

IT Body weight
(loss; variations in preproghrelin gene correlated with insulin resistance, altered blood lipids, higher body mass index, fat mass, and body dissatisfaction in young Japanese women)

IT 50-99-7, D-Glucose, biological studies 57-88-5, Cholesterol, biological studies 304853-26-7D, Ghrelin, acylated
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(variations in preproghrelin gene correlated with insulin resistance, altered blood lipids, higher body mass index, fat mass, and body dissatisfaction in young Japanese women)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 33 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:821729 CAPLUS Full-text
DOCUMENT NUMBER: 145:288954
TITLE: Regulation of food intake by acyl and des-acyl ghrelins in the goldfish
AUTHOR(S): Matsuda, Kouhei; Miura, Tohru; Kaiya, Hiroyuki; Maruyama, Keisuke; Shimakura, Sei-Ichi; Uchiyama, Minoru; Kangawa, Kenji; Shioda, Seiji
CORPORATE SOURCE: Laboratory of Regulatory Biology, Graduate School of Science and Engineering, University of Toyama, Toyama, 930-8555, Japan
SOURCE: Peptides (New York, NY, United States) (2006), 27(9), 2321-2325
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors' recent research has indicated that intracerebroventricular (ICV) and i.p. (IP) administration of n-octanoic acid-modified ghrelin (acyl ghrelin) stimulates food intake and locomotor activity in the goldfish. The manner in which peripherally administered acyl ghrelin regulates food intake, however, remains unclear. In contrast to acyl ghrelin, non-acylated ghrelin (des-acyl ghrelin) does not exert an orexigenic action or induce hypermotility. To this extent, the biol. role of des-acyl ghrelin in fish is unknown. Given the possible involvement of afferent pathways in mediating the effects of acyl ghrelin, as is known to occur in rodents, the authors examined the effect of capsaicin, a neurotoxin which destroys primary sensory (vagal and splanchnic) afferents, on the orexigenic activity induced by IP-injected acyl ghrelin. Pretreatment with IP-injected capsaicin (0.16 μmol/g body weight (BW)) cancelled the orexigenic action of IP-injected acyl ghrelin (8 pmol/g BW), although IP-injected capsaicin alone did not affect food intake. The effect of des-acyl ghrelin on the orexigenic action of acyl ghrelin in the goldfish was also investigated. The ICV and IP injection of des-acyl ghrelin at doses 3-10 times higher than that of acyl ghrelin suppressed the orexigenic action of ICV- and IP-injected acyl ghrelin (doses of 1 and 8 pmol/g BW). In contrast, injection of des-acyl ghrelin alone did not show any inhibitory effect on food intake. These results suggest that, as is seen in rodents, circulating acyl ghrelin derived from peripheral tissues acts via primary sensory afferent pathways on feeding centers in the brain. The results also

show that des-acyl ghrelin inhibits acyl ghrelin-induced orexigenic activity in goldfish.

CC 12-6 (Nonmammalian Biochemistry)

ST goldfish des acyl ghrelin appetite sensory afferent

IT Appetite
Carassius auratus
(regulation of food intake by acyl and des-acyl ghrelins in the goldfish)

IT 304853-26-7D, Ghrelin, des-n-octanoylated 304853-26-7D, Ghrelin, n-octanoylated
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(regulation of food intake by acyl and des-acyl ghrelins in the goldfish)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 34 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1210223 CAPLUS Full-text
DOCUMENT NUMBER: 146:356416
TITLE: Differential effects of gastric bypass and banding on circulating gut hormone and leptin levels
AUTHOR(S): Korner, Judith; Inabnet, William; Conwell, Irene M.; Taveras, Carmen; Daud, Amna; Olivero-Rivera, Lorraine; Restuccia, Nancy L.; Bessler, Marc
CORPORATE SOURCE: Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, NY, USA
SOURCE: Obesity (2006), 14(9), 1553-1561
CODEN: OBESAX; ISSN: 1930-7381
PUBLISHER: North American Association for the Study of Obesity
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: To quantify plasma concns. of hormones that regulate energy homeostasis in order to establish possible mechanisms for greater weight loss after Roux-en-Y gastric bypass (RYGBP) compared with gastric banding (BND). Research Methods and Procedures: Four groups of women were studied: lean (n = 8; mean BMI, 21.6 kg/m2); BND (n = 9; BMI, 35.8; 25% weight loss), RYGBP (n = 9; BMI, 34.2; 36% weight loss), and controls matched for BMI to the surgical groups (n = 11; BMI, 34.4). Results: Fasting total peptide YY (PYY) and PYY(3-36) immunoreactivity were similar among all groups, but the postprandial response in the RYGBP group was exaggerated, such that 30 min after the meal, total and PYY(3-36) levels were 2- to 4-fold greater compared with all other groups. Maximal postprandial suppression of total ghrelin was blunted in the BND group (13%) compared with RYGBP (27%). Postprandial suppression of octanoylated ghrelin was also less in BND (29%) compared with RYGBP (56%). Fasting insulin was lower in RYGBP (6.6 μU/mL) compared with BND (10.0 μU/mL). Compared with lean controls, leptin concns. were significantly higher in BND but not in RYGBP. There was a greater increase in post-meal satiety in the RYGBP group compared with BND and overweight controls. Discussion: The differences between RYGBP and BND subjects in postprandial concns. of PYY and ghrelin would be expected to promote increased satiety and earlier meal termination in RYGBP and may aid in greater weight loss. The differences in insulin and leptin concns. associated with these procedures may also reflect differences in insulin sensitivity and energy partitioning.

CC 14-14 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2

IT Blood plasma
Body weight
Human
Hunger
Obesity

Postprandial period
(differential effects of gastric bypass and banding on circulating gut hormone and leptin levels)
IT Body weight
(loss; differential effects of gastric bypass and banding on circulating gut hormone and leptin levels)
IT Appetite
(satiety; differential effects of gastric bypass and banding on circulating gut hormone and leptin levels)
IT 169494-85-3, Leptin 304853-26-7, Ghrelin 304853-26-7D, Ghrelin, octanoylated
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(differential effects of gastric bypass and banding on circulating gut hormone and leptin levels)
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 35 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:521474 CAPLUS Full-text
DOCUMENT NUMBER: 144:487839
TITLE: Carob pulp preparation rich in insoluble dietary fiber and polyphenols enhances lipid oxidation and lowers postprandial acylated ghrelin in humans
AUTHOR(S): Gruendel, Sindy; Garcia, Ada L.; Otto, Baerbel; Mueller, Corinna; Steiniger, Jochen; Weickert, Martin O.; Speth, Maria; Katz, Norbert; Koebnick, Corinna
CORPORATE SOURCE: Dietary Fibre and the Metabolic Syndrome Group, German Institute of Human Nutrition Potsdam-Rehbruecke, Nuthetal, Germany
SOURCE: Journal of Nutrition (2006), 136(6), 1533-1538
CODEN: JONUAI; ISSN: 0022-3166
PUBLISHER: American Society for Nutrition
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ghrelin is an orexigenic hormone that may affect substrate utilization in humans. Ghrelin is influenced by macronutrients, but the effects of insol. dietary fiber and polyphenols are unknown. We investigated the effects of a polyphenol-rich insol. dietary fiber preparation from carob pulp (carob fiber) on postprandial ghrelin responses and substrate utilization. Dose-dependent effects of the consumption of carob fiber were investigated in a randomized, single-blind, crossover study in 20 healthy subjects, aged 22-62 yr. Plasma total and acylated ghrelin, triglycerides, and serum insulin and nonesterified fatty acids (NEFA) levels were repeatedly assessed before and after ingestion of an isocaloric standardized liquid meal with 0, 5, 10, or 20 g of carob fiber over a 300-min period. The RQ was determined after consumption of 0 or 20 g of carob fiber. Carob fiber intake lowered acylated ghrelin to 49.1%, triglycerides to 97.2%, and NEFA to 67.2% compared with the control meal ($P < 0.001$). Total ghrelin and insulin concns. were not affected by consumption of a carob fiber-enriched liquid meal. Postprandial energy expenditure was increased by 42.3% and RQ was reduced by 99.9% after a liquid meal with carob fiber compared with a control meal ($P < 0.001$). We showed that the consumption of a carob pulp preparation, an insol. dietary fiber rich in polyphenols, decreases postprandial responses of acylated ghrelin, triglycerides, and NEFA and alters RQ, suggesting a change toward increased fatty acid oxidation These results indicate that carob fiber might exert beneficial effects in energy intake and body weight
CC 18-4 (Animal Nutrition)
IT Blood plasma
Blood serum
Body weight

Ceratonia siliqua
Dietary fiber
Dietary supplements
Energy metabolism, animal
Human
Lipid oxidation
Postprandial period
Respiration, animal
(carob pulp preparation rich in insol. dietary fiber and polyphenols enhances lipid oxidation and lowers postprandial acylated ghrelin in humans)
IT 50-99-7, D-Glucose, biological studies 9004-10-8, Insulin, biological studies 304853-26-7, Ghrelin 304853-26-7D, Ghrelin, acylated
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(carob pulp preparation rich in insol. dietary fiber and polyphenols enhances lipid oxidation and lowers postprandial acylated ghrelin in humans)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 36 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:517379 CAPLUS Full-text
DOCUMENT NUMBER: 145:59635
TITLE: Stimulatory effect of n-octanoylated ghrelin on locomotor activity in the goldfish, Carassius auratus
AUTHOR(S): Matsuda, Kouhei; Miura, Tohru; Kaiya, Hiroyuki; Maruyama, Keisuke; Uchiyama, Minoru; Kangawa, Kenji; Shioda, Seiji
CORPORATE SOURCE: Laboratory of Regulatory Biology, Graduate School of Science and Engineering, University of Toyama, Toyama, 930-8555, Japan
SOURCE: Peptides (New York, NY, United States) (2006), 27(6), 1335-1340
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ghrelin is implicated in growth and feeding regulation in fish. The influence of ghrelin on behavior has not been well studied and the physiol. role of des-fatty acid modification of this peptide is unclear. Therefore, the effects of intracerebroventricular (ICV) and i.p. (IP) administration of synthetic n-octanoylated (acyl) goldfish ghrelin and des-n-octanoylated (des-acyl) ghrelin on locomotor and orexigenic activity in the goldfish were examined ICV administration of acyl ghrelin at doses of 1 and 2 pmol/g body weight (BW) and IP administration at 16 pmol/g BW both induced significant increases in locomotor activity during for 45-60 min after treatment. Cumulative food intake was significantly increased by ICV injection of acyl ghrelin at doses of 1 and 2 pmol/g BW and IP injection at 8 and 16 pmol/g BW during the 60-min post-treatment observation period. In contrast, ICV and IP administration of des-acyl ghrelin produced no changes in locomotor and orexigenic activity. The authors also analyzed fasting-induced changes in the expression of ghrelin mRNA in the brain and intestine using a real-time PCR method. The level of ghrelin mRNA in the intestine, but not in the brain, obtained from fish fasted for 7 days was significantly higher than that in fish that had been fed normally. These results suggest that, in the goldfish, acyl ghrelin, but not des-acyl ghrelin, stimulates locomotor activity and enhances food intake via central and peripheral pathways.
CC 12-6 (Nonmammalian Biochemistry)
ST goldfish ghrelin locomotor behavior appetite
IT Appetite

Brain
Carassius auratus
Fasting
Intestine
(stimulatory effect of n-octanoylated ghrelin on locomotor activity in the goldfish)

IT 304853-26-7D, Ghrelin, des-n-octanoylated 304853-26-7D, Ghrelin, n-octanoylated
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(stimulatory effect of n-octanoylated ghrelin on locomotor activity in the goldfish)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 37 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:764163 CAPLUS Full-text
DOCUMENT NUMBER: 146:7036
TITLE: Physiogenomic analysis of weight loss induced by dietary carbohydrate restriction
AUTHOR(S): Ruano, Gualberto; Windemuth, Andreas; Kocherla, Mohan; Holford, Theodore; Fernandez, Maria Luz; Forsythe, Cassandra E.; Wood, Richard J.; Kraemer, William J.; Volek, Jeff S.
CORPORATE SOURCE: Genomas, Inc., Hartford, CT, 06106, USA
SOURCE: Nutrition & Metabolism (2006), 3, No pp. given
CODEN: NMUEAZ; ISSN: 1743-7075
URL: http://www.nutritionandmetabolism.com/content/pdf/1743-7075-3-20.pdf
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background: Diets that restrict carbohydrate (CHO) have proven to be a successful dietary treatment of obesity for many people, but the degree of weight loss varies across individuals. The extent to which gentic factors associate with the magnitude of weight loss induced by CHO restriction is unknown. The authors examined assocns. among polymorphisms in candidate genes and weight loss to understand the physiol. factors influencing body weight responses to CHO restriction. Methods: The authors screened for genetic assocns. with weight loss in 86 healthy adults who were instructed to restrict CHO to a level that induced a small level of ketosis (CHO .apprx.10% of total energy). A total of 27 single nucleotide polymorphisms (SNPs) were selected from 15 candidate genes involved in fat digestion/metabolism, intracellular glucose metabolism, lipoprotein remodeling, and appetite regulation. Multiple linear regression was used to rank the SNPs according to probability of association, and the most significant assocns. were analyzed in greater detail. Results: Mean weight loss was 6.4 kg. SNPs in the gastric lipase (LIPF), hepatic glycogen synthase (GYS2), cholesteryl ester transfer protein (CETP) and galanin (GAL) genes were significantly associated with weight loss. Conclusion: A strong association between weight loss induced by dietary CHO restriction and variability in genes regulating fat digestion, hepatic glucose metabolism, intravascular lipoprotein remodeling, and appetite were detected. These discoveries could provide clues to important physiol. adaptations underlying the body mass response to CHO restriction.

CC 18-4 (Animal Nutrition)

IT Body weight
(loss; physiogenomics of weight loss induced by dietary carbohydrate restriction)

IT 9001-62-1, Lipase 9004-02-8, Lipoprotein lipase 9014-56-6, Glycogen synthase 9026-00-0, Lysosomal acid lipase 9043-29-2, Endothelial lipase 82785-45-3, Neuropeptide Y 119418-04-1, Galanin

304853-26-7D, Ghrelin, precursor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(physiogenomics of weight loss induced by dietary carbohydrate restriction)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 38 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1329098 CAPLUS Full-text
DOCUMENT NUMBER: 144:45727
TITLE: Ghrelin regulator comprising C6-12 or C8-10 fatty acids or derivatives for food and pharmaceutical use
INVENTOR(S): Kojima, Masayasu; Nishi, Yoshihiro; Kangawa, Kenji; Abe, Keiichi; Izumi, Reiko; Nakamura, Junichi
PATENT ASSIGNEE(S): Kurume University, Japan; Suntory Limited
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005120485	A1	20051222	WO 2005-JP7465	20050419
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2005120484	A1	20051222	WO 2004-JP15413	20041019
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005251576	A1	20051222	AU 2005-251576	20050419
CA 2569678	A1	20051222	CA 2005-2569678	20050419
EP 1767198	A1	20070328	EP 2005-734737	20050419
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
KR 2007043710	A	20070425	KR 2006-725994	20061208
PRIORITY APPLN. INFO.:			JP 2004-171245 A	20040609
			WO 2005-JP7465 W	20050419

AB A regulator for regulating the physiol. functions, such as activity of increasing an intracellular calcium ion concentration, activity of promoting growth hormone secretion, activity of promoting eating, regulatory activity

relating to fat accumulation, activity of ameliorating heart function and activity of stimulating gastric acid secretion, of ghrelin, which regulator comprises a C2-35 fatty acids or their derivs. These ghrelin regulators are useful as functional food (or feed) and pharmaceutical to e.g. enhance phys. strength and beautify skin.

IC ICM A61K031-19
ICS A61K031-20; A61K031-22; A61K031-23; A61P001-04; A61P001-14; A61P003-00; A61P003-02; A61P003-04; A61P005-08; A61P009-00; A61P017-02; A61P019-02; A61P019-10; A23L001-30

CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 5, 17, 18, 63

IT Animals
Anorexia
Domestic animal
Drug delivery systems
Drugs
Feed
Feed additives
Food
Food additives
Human
Malnutrition
Mammalia
(ghrelin regulator comprising C6-12 or C8-10 fatty acids or derivs. for food and pharmaceutical use)

IT 304853-26-7D, Ghrelin, acylated derivs.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ghrelin regulator comprising C6-12 or C8-10 fatty acids or derivs. for food and pharmaceutical use)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 39 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1259412 CAPLUS Full-text
DOCUMENT NUMBER: 144:21844
TITLE: Immunotherapy of obesity and appetite disorders
INVENTOR(S): Charlton, Keith; Porter, Andrew; Strachan, Gillian
PATENT ASSIGNEE(S): Haptogen Ltd., UK
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005113600	A2	20051201	WO 2005-GB1916	20050518
WO 2005113600	A3	20060608		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,

RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2004-11014 A 20040518
OTHER SOURCE(S): MARPAT 144:21844

AB The authors disclose methods for regulating food intake and weight gain/loss by selectively modulating the extracellular concentration of endogenous cannabinoid and digestive tract hormones. In one example, arachidonic acid derivs. are conjugated to carrier proteins and used to elicit rodent antibodies or to select antibodies from human libraries/. Furthermore, the conjugates may have application as vaccines.

IC ICM C07K016-00
CC 15-3 (Immunochemistry)
Section cross-reference(s): 14
ST antibody endocannabinoid immunotherapy obesity appetite disorder; ghrelin antibody immunotherapy obesity appetite disorder; neuropeptide Y antibody immunotherapy obesity appetite disorder

IT Antiobesity agents
Appetite depressants
Appetite stimulants
(antibodies to endocannabinoids or digestive tract hormones derivs.)

IT Human
(antibodies to endocannabinoids or digestive tract hormones derivs. for immunotherapy of obesity or appetite disorders)

IT Cannabinoids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(endocannabinoids; antibodies to endocannabinoids or digestive tract hormones derivs. for immunotherapy of obesity or appetite disorders)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; to endocannabinoids or digestive tract hormones derivs. for immunotherapy of obesity or appetite disorders)

IT Phage display library
(of antibodies to endocannabinoids or digestive tract hormones derivs. for immunotherapy of obesity or appetite disorders)

IT Vaccines
(of endocannabinoids or digestive tract hormones derivs. for immunotherapy of obesity or appetite disorders)

IT Immunotherapy
(of obesity or appetite disorders)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(single chain, 3AB12, 4AD8, 3BE10 or 3BH10; to endocannabinoids or digestive tract hormones derivs. for immunotherapy of obesity or appetite disorders)

IT 53847-30-6, 2-Arachidonylglycerol 94421-68-8, Anandamide 106388-42-5, Peptide YY 304853-26-7D, Ghrelin, derivs. 307950-60-3D, 3-acylserine derivs. 313951-59-6D, 3-acylserine derivs. 869989-42-4D, 3-acylserine derivs. 869989-43-5D, 3-acylserine derivs. 870491-48-8 870491-49-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(antibodies to endocannabinoids or digestive tract hormones derivs. for immunotherapy of obesity or appetite disorders)

L99 ANSWER 40 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1239564 CAPLUS Full-text

DOCUMENT NUMBER: 144:945
TITLE: Methods of inhibiting proinflammatory cytokine expression using ghrelin
INVENTOR(S): Dixit, Vishwa Deep; Taub, Dennis D.
PATENT ASSIGNEE(S): The Government of the United States of America, As Represented by the Secretary Department of Health and Human Services National Institutes of Health, USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110463	A1	20051124	WO 2005-US16565	20050511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2566703	A1	20051124	CA 2005-2566703	20050511
EP 1750745	A1	20070214	EP 2005-747960	20050511
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: US 2004-569819P P 20040511
WO 2005-US16565 W 20050511

AB The present invention provides a method of inhibiting proinflammatory cytokine expression using ghrelin. Also provided by the invention is a method of treating loss of appetite and sepsis comprising administering ghrelin or a fragment thereof.

IC ICM A61K038-17
ICS A61P029-00; A61P003-00; A61P031-00

CC 2-6 (Mammalian Hormones)

ST inflammation inhibition sepsis appetite disorder treatment ghrelin

IT Asthma
Autoimmune disease
Burn
Hepatotoxicity
Mycosis
Neoplasm
Transplant rejection
(inflammation associated with; methods of inhibiting proinflammatory cytokine expression using ghrelin, its cDNA, and fragments thereof)

IT Anorexia
Appetite stimulants
Eating disorders
(method of treating loss of appetite with ghrelin)

IT 304853-26-7, Ghrelin 304853-26-7D, Ghrelin, fragments
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods of inhibiting proinflammatory cytokine expression using ghrelin, its cDNA, and fragments thereof)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 41 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1103612 CAPLUS Full-text
DOCUMENT NUMBER: 143:385164
TITLE: Antibody specific to mammalian endogenous ligand without neutralizing activity for stabilizing ligand and enhancing receptor activity to treat diseases
INVENTOR(S): Inooka, Hiroshi; Suzuki, Nobuhiro; Kokubo, Toshio; Kurokawa, Tomofumi
PATENT ASSIGNEE(S): Takeda Pharmaceutical Company Limited, Japan
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005094881	A1	20051013	WO 2005-JP6576	20050329
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2561732	A1	20051013	CA 2005-2561732	20050329
EP 1731168	A1	20061213	EP 2005-721715	20050329
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
US 2007202099	A1	20070830	US 2006-594773	20060929

PRIORITY APPLN. INFO.: JP 2004-98595 A 20040330
WO 2005-JP6576 W 20050329

AB An ameliorating agent for the stability of mammalian endogenous ligand in the blood, comprising an antibody having affinity with mammalian endogenous ligand and substantially not neutralizing the same; and prepns. thereof for the prevention and treatment of diseases in accomplishment of which it is effective to increase the concentration of endogenous ligand in the blood and/or prolong the half life period thereof in the blood. When the prepns. alone without being combined with a compound identical with or substantially identical with the endogenous ligand are administered to a mammal, the stability of endogenous ligand in the blood would be enhanced to thereby reinforce the receptor activity regulating action thereof. The endogenous ligand belonging to the secretin/glucagon superfamily is selected from GLP-1, calcitonin, PACAP, VIP, LHRH, metastin, GPR7/GPR8 ligand, MSH, ghrelin, apelin, EPO, TPO, insulin, interferon, growth hormone, GM-CSF, leptin, adiponectin, ANP, BNP, CNP, betacellulin, betacellulin-γ4, adrenomedullin.

IC ICM A61K039-395
ICS A61K047-48; A61P003-00; A61P005-02; A61P005-06; A61P005-18; A61P005-48; A61P007-00; A61P009-00; A61P015-00; A61P015-10; A61P015-18; A61P019-08; A61P025-00; A61P031-00; A61P035-00;

A61P037-04
CC 15-3 (Immunochemistry)
Section cross-reference(s): 2
IT Affinity
Antiserums
Antitumor agents
Blood, disease
Bone, disease
Brain, disease
Cartilage, disease
Fertility disorders
Growth disorders, animal
Immunodeficiency
Infection
Mammalia
Metabolic disorders
Neoplasm
Stabilizing agents
Urinary system, disease
(antibody specific to mammalian endogenous ligand without neutralizing activity to stabilize ligand and enhance receptor activity for treating diseases)
IT 1393-25-5D, Secretin, analogs 9002-72-6D, Growth hormone, analogs 9002-79-3D, MSH, analogs 9004-10-8D, Insulin, analogs 9007-12-9D, Calcitonin, analogs 9007-92-5D, Glucagon, analogs 9014-42-0D, Thrombopoietin, analogs 9034-40-6D, LHRH, analogs 11096-26-7D, EPO, analogs 37221-79-7D, VIP, analogs 83869-56-1D, GM-CSF, analogs 85637-73-6D, Atrial natriuretic polypeptide, analogs 89750-14-1D, Glucagon-like peptide I, analogs 114471-18-0D, Brain natriuretic peptide, analogs 127830-04-0D, C-type natriuretic peptide, analogs 137061-48-4D, PACAP, analogs 154835-90-2D, Adrenomedullin, analogs 163150-12-7D, Betacellulin, γ4 analogs 169494-85-3D, Leptin, analogs 304853-26-7D, Ghrelin, analogs 372170-33-7D, Apelin, analogs 388138-21-4D, Metastin, analogs
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody specific to mammalian endogenous ligand without neutralizing activity to stabilize ligand and enhance receptor activity for treating diseases)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 42 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:673405 CAPLUS Full-text
DOCUMENT NUMBER: 143:171311
TITLE: Modified ghrelin peptide-VLP (virus-like particle) carrier conjugates, and immunogenic uses for the treatment of obesity
INVENTOR(S): Bachmann, Martin F.; Fulurija, Alma
PATENT ASSIGNEE(S): Cytos Biotechnology A. G., Switz.
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005068639	A2	20050728	WO 2005-EP497	20050119

WO 2005068639	A3	20060202			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2005205181	A1	20050728	AU 2005-205181		20050119
CA 2553594	A1	20050728	CA 2005-2553594		20050119
US 2005191317	A1	20050901	US 2005-37396		20050119
EP 1706152	A2	20061004	EP 2005-701048		20050119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS					
CN 1905903	A	20070131	CN 2005-80001759		20050119
BR 2005007002	A	20070605	BR 2005-7002		20050119
JP 2007518762	T	20070712	JP 2006-550027		20050119
IN 2006MN00834	A	20070323	IN 2006-MN834		20060714
MX 2006PA08170	A	20061002	MX 2006-PA8170		20060718
PRIORITY APPLN. INFO.:			US 2004-537230P	P	20040120
			WO 2005-EP497	W	20050119

AB The inventors found that particular ghrelin-peptides, which are bound to a core particle having a structure with an inherent repetitive organization, in particular to virus-like-particles (VLPs), particularly when leading to highly ordered and repetitive conjugates, represent potent immunogens for the induction of specific antibody response against ghrelin. The invention provides a modified VLP comprising a VLP, derived from a bacteriophage, and particular peptides derived from ghrelin linked thereto, wherein said ghrelin-peptide does not contain a n-octanoyl-modification. The invention also provides a process for producing the modified ghrelin peptide-VLP. The modified ghrelin peptide-VLPs of the invention are useful in the production of safe vaccines for the treatment of obesity and other disease associated with increased food-uptake or increased body weight and to efficiently induce immune responses, in particular antibody responses. Thus, the inventors found that peptide 1-6, peptide 1-7 and peptide 1-8 coupled to VLPs constitute safe vaccines with the surprising ability to induce potent antibody responses cross-reacting with native ghrelin. Furthermore, the inventors found that surprisingly a ghrelin-peptide coupled via its C-terminus to the virus-like particles was far more potent at reducing body weight-increase than a ghrelin-peptide coupled via its N-terminus to the VLP.
IC ICM C12N015-86
ICS A61K047-48
CC 15-2 (Immunochemistry)
Section cross-reference(s): 1, 2, 63
IT Body weight
(increased, control of; modified ghrelin peptide-VLP (virus-like particle) carrier conjugates, and immunogenic uses for treatment of obesity)
IT 304853-26-7D, Ghrelin, peptide-VLP conjugates
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modified ghrelin peptide-VLP (virus-like particle) carrier conjugates, and immunogenic uses for treatment of obesity)

L99 ANSWER 43 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:269024 CAPLUS Full-text
DOCUMENT NUMBER: 142:310203
TITLE: Effect of centrally administered C75, a fatty acid synthase inhibitor, on ghrelin secretion and its downstream effects
AUTHOR(S): Hu, Zhiyuan; Cha, Seung Hun; Van Haasteren, Goedelle; Wang, Jing; Lane, M. Daniel
CORPORATE SOURCE: Department of Biological Chemistry, The Johns Hopkins University School of Medicine, Baltimore, MD, 21205, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2005), 102(11), 3972-3977
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The central administration of the fatty acid synthase (FAS) inhibitor, C75, rapidly suppresses the expression of orexigenic neuropeptides [neuropeptide Y (NPY) and agouti-related protein (AgRP)] and activates expression of anorexigenic neuropeptides [proopiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART)] in the hypothalamus. The combined actions of these changes inhibit food intake and decrease body weight Intracerebroventricular injection of C75 appears to rapidly inhibit the secretion of ghrelin by hypothalamic explants ex vivo and by the stomach in vivo. Ghrelin administered intracerebroventricularly reverses the anorexic effect of C75, suggesting that C75 acts upstream of ghrelin. Because ghrelin-producing neurons are known to form synapses onto NPY/AgRP neurons, the authors suggest that the reversal of C75-induced anorexia by ghrelin may be mediated by NPY/AgRP neurons. This hypothesis is supported by the finding that ghrelin reverses the C75-induced inactivation (assessed by c-Fos expression) of neurons in the arcuate nucleus that express NPY (assessed by immunohistochem. costaining). These effects closely correlate with appropriate changes down-stream in the expression of the hypothalamic neuropeptides that regulate feeding behavior, i.e., down-regulation of the expression of NPY and AgRP and up-regulation of the expression of proopiomelanocortin/α-MSH, provoked by C75 and reversed by ghrelin. The authors propose a model in which ghrelin secretion plays an intermediary role between malonyl-CoA, the substrate of fatty acid synthase, and the neural circuitry regulating energy homeostasis.

CC 2-6 (Mammalian Hormones)
ST fatty acid synthase brain ghrelin hypothalamus neuropeptide appetite
IT Anorexia
Appetite
Body weight
Brain
Energy.metabolism, animal
Stomach
(centrally administered fatty acid synthase inhibitor effect on ghrelin secretion and its downstream effects)
IT 524-14-1, Malonyl-CoA 9045-77-6, Fatty acid synthase 37213-49-3, α-MSH 66796-54-1, Proopiomelanocortin 82785-45-3, Neuropeptide Y 304853-26-7, Ghrelin 304853-26-7D, Ghrelin, des-n-octanoyl derivs.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(centrally administered fatty acid synthase inhibitor effect on ghrelin secretion and its downstream effects)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 44 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:473171 CAPLUS Full-text
DOCUMENT NUMBER: 143:38596
TITLE: Molecular forms of hypothalamic ghrelin and its regulation by fasting and 2-deoxy-D-glucose administration
AUTHOR(S): Sato, Takahiro; Fukue, Yoshihiko; Teranishi, Hitoshi; Yoshida, Yayoi; Kojima, Masayasu
CORPORATE SOURCE: Molecular Genetics, Institute of Life Sciences, Kurume University, Fukuoka, 839-0864, Japan
SOURCE: Endocrinology (2005), 146(6), 2510-2516
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ghrelin, an endogenous ligand for the GH secretagogue receptor, is a hormone expressed in stomach and other tissues, such as hypothalamus, testis, and placenta. This hormone acts at a central level to stimulate GH secretion and food intake. Little is known, however, about the mol. forms and physiol. roles of ghrelin within the hypothalamus. The authors detail the mol. forms, mRNA expression patterns, and peptide contents of ghrelin within the rat hypothalamus. Using the combination of reverse-phase HPLC and ghrelin-specific RIA, the authors determined that the rat hypothalamus contains both n-octanoyl-modified and des-acyl ghrelins. Fasting for 24 and 48 h significantly decreased ghrelin mRNA expression in the hypothalamus to 24% and 28% of control values, resp. Both n-octanoyl-modified and des-acyl ghrelin content in the hypothalamus decreased after 24 and 48 h of fasting. These results contrast the changes in gastric ghrelin after fasting, which decreased in content despite increased mRNA expression. Two hours after injection of 2-deoxy-D-glucose (2-DG), a selective blocker of carbohydrate metabolism, ghrelin peptide levels also decreased. Thus, induction of glucoprivic states, such as fasting and 2-DG treatment, decreased ghrelin gene expression and peptide content within the hypothalamus.

CC 2-6 (Mammalian Hormones)
Section cross-reference(s): 18
IT Appetite
Fasting
Stomach
(mol. forms of hypothalamic ghrelin and its regulation in glucoprivation by fasting and deoxyglucose administration)
IT 50-99-7, D-Glucose, biological studies 67382-96-1, Melanin-concentrating hormone 82785-45-3, Neuropeptide Y 304853-26-7, Ghrelin 304853-26-7D, Ghrelin, n-octanoyl-modified and des-acyl derivs.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mol. forms of hypothalamic ghrelin and its regulation in glucoprivation by fasting and deoxyglucose administration)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 45 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:59399 CAPLUS Full-text
DOCUMENT NUMBER: 142:132304
TITLE: Effects of Roux-en-Y gastric bypass surgery on fasting and postprandial concentrations of plasma ghrelin, peptide YY, and insulin
AUTHOR(S): Korner, Judith; Bessler, Marc; Cirilo, L. J.; Conwell, Irene M.; Daud, Amna; Restuccia, Nancy L.; Wardlaw, Sharon L.
CORPORATE SOURCE: Department of Medicine, College of Physicians & Surgeons, Columbia University, New York, NY, 10032,

USA
SOURCE: Journal of Clinical Endocrinology and Metabolism (2005), 90(1), 359-365
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To help understand the mechanisms by which weight loss is maintained after Roux-en-Y gastric bypass (RYGBP), we measured circulating concns. of total and bioactive octanoylated ghrelin, peptide YY (PYY), glucose, and insulin in the fasted state and in response to a liquid test meal in three groups of adult women: lean (n = 8); weight-stable 35 ± 5 mo after RYGBP (n = 12; mean body mass index, 33 kg/m2); and matched to the surgical group for body mass index and age (n = 12). Fasting plasma total ghrelin levels were nearly identical between RYGBP (425 ± 54 pg/mL) and the matched controls (424 ± 28 pg/mL) and highest in lean controls (564 ± 103 pg/mL). The response to the test meal was comparable between lean and RYGBP groups, with 27% and 20% maximal suppression, resp., whereas the magnitude of suppression was significantly diminished in the matched controls (17%) compared with the lean group. Fasting levels of octanoylated ghrelin were highest in the lean controls, 220 ± 36 pg/mL vs. 143 ± 27 in the RYGBP group (P = 0.05) and 127 ± 12 pg/mL in the matched controls (P < 0.05). The magnitude of maximal post-meal suppression of octanoylated ghrelin was more marked than with total ghrelin, but similar among groups, ranging from 44-47%. In response to the test meal, there was an early exaggerated rise in PYY in the RYGBP group, such that the peak PYY concentration was 163 ± 24 pg/mL compared with 58 ± 17 (P < 0.01) and 77 ± 23 (P < 0.05) in the matched and lean controls, resp.; area under the curve at 90 min was significantly greater compared with both control groups. Leptin and fasting insulin concns. and homeostasis model of assessment insulin resistance indexes were nearly identical between lean and RYGBP subjects and significantly higher in the body mass index-matched controls. In summary, the absence of a compensatory increase in ghrelin concns. that usually occurs with diet-induced weight loss, and the exaggerated postprandial PYY response after RYGBP, may contribute to weight loss and to the ability of an individual to maintain weight loss after this surgical procedure.

CC 14-14 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2

IT Body weight
(loss; Roux-en-Y gastric bypass surgery effect on fasting and postprandial plasma ghrelin, peptide YY, and insulin)

IT Appetite
(satiety; Roux-en-Y gastric bypass surgery effect on fasting and postprandial plasma ghrelin, peptide YY, and insulin)

IT 9004-10-8, Insulin, biological studies 106388-42-5, Peptide YY 169494-85-3, Leptin 304853-26-7, Ghrelin 304853-26-7D, Ghrelin, octanoylated
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Roux-en-Y gastric bypass surgery effect on fasting and postprandial plasma ghrelin, peptide YY, and insulin)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 46 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:2387 CAPLUS Full-text
DOCUMENT NUMBER: 142:86880
TITLE: Transgenic mice overexpressing des-acyl ghrelin show small phenotype
AUTHOR(S): Ariyasu, Hiroyuki; Takaya, Kazuhiko; Iwakura, Hiroshi; Hosoda, Hiroshi; Akamizu, Takashi; Arai, Yuji; Kanagawa, Kenji; Nakao, Kazuwa

CORPORATE SOURCE: Dep. Med. Clinical Sci., Kyoto Univ. Grad. Sch. Med., Kyoto, 606-8507, Japan
SOURCE: Endocrinology (2005), 146(1), 355-364
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ghrelin, a 28-amino acid acylated peptide, displays strong GH-releasing activity in concert with GHRH. The fatty acid modification of ghrelin is essential for the actions, and des-acyl ghrelin, which lacks the modification, has been assumed to be devoid of biol. effects. Some recent reports, however, indicate that des-acyl ghrelin has effects on cell proliferation and survival. In the present study, the authors generated two lines of transgenic mice bearing the preproghrelin gene under the control of chicken β-actin promoter. Transgenic mice overexpressed des-acyl ghrelin in a wide variety of tissues, and plasma des-acyl ghrelin levels reached 10- and 44-fold of those in control mice. They exhibited lower body wts. and shorter nose-to-anus lengths, compared with control mice. The serum GH levels tended to be lower, and the serum IGF-I levels were significantly lower in both male and female transgenic mice than control mice. The responses of GH to administered GHRH were normal, whereas those to administered ghrelin were reduced, especially in female transgenic mice, compared with control mice. These data suggest that overexpressed des-acyl ghrelin may modulate the GH-IGF-I axis and result in small phenotype in transgenic mice.

CC 2-6 (Mammalian Hormones)

IT Appetite
Blood plasma
Body weight
Cell proliferation
Development, mammalian postnatal
Growth, animal
Heart
Kidney
Sex
Stomach
(des-acyl ghrelin effect on growth and GH-IGF axis and other factors in transgenic mice)

IT 9002-60-2, ACTH, biological studies 9002-67-9, LH 9002-68-0, FSH 9002-71-5, TSH 9002-72-6, Growth hormone 9004-10-8, Insulin, biological studies 9034-39-3, Somatoliberin 51110-01-1, Somatostatin 67763-96-6, IGF-I 304853-26-7, Ghrelin 304853-26-7D, Ghrelin, des-acyl derivs.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(des-acyl ghrelin effect on growth and GH-IGF axis and other factors in transgenic mice)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 47 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1152686 CAPLUS Full-text
DOCUMENT NUMBER: 144:812
TITLE: A Novel Growth Hormone Secretagogue-1a Receptor Antagonist That Blocks Ghrelin-Induced Growth Hormone Secretion but Induces Increased Body Weight Gain
AUTHOR(S): Halem, Heather A.; Taylor, John E.; Dong, Jesse Z.; Shen, Yeelana; Datta, Rakesh; Abizaid, Alfonso; Diano, Sabrina; Horvath, Tamas L.; Culler, Michael D.
CORPORATE SOURCE: IPSEN Group, Milford, MA, USA
SOURCE: Neuroendocrinology (2005), 81(5), 339-349
CODEN: NUNDAJ; ISSN: 0028-3835

PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ghrelin, the natural ligand for the growth hormone secretagogue-1a (GHS-1a) receptor, has received a great deal of attention due to its ability to stimulate weight gain and the hope that an antagonist of the GHS-1a receptor could be a treatment for obesity. We have discovered an analog of full-length human ghrelin, BIM-28163, which fully antagonizes GHS-1a by binding to but not activating the receptor. We further demonstrate that BIM-28163 blocks ghrelin activation of the GHS-1a receptor, and inhibits ghrelin-induced GH secretion in vivo. Unexpectedly, however, BIM-28163 acts as an agonist with regard to stimulating weight gain. These results may suggest the presence of an unknown ghrelin receptor that modulates ghrelin actions on weight gain. In keeping with our results on growth hormone (GH) secretion, BIM-28163 acts as an antagonist of ghrelin-induced Fos protein immunoreactivity (Fos-IR) in the medial arcuate nucleus, an area involved in the ghrelin modulation of GH secretion. However, in the dorsal medial hypothalamus (DMH), a region associated with regulation of food intake, both ghrelin and BIM-28163 act as agonists to upregulate Fos-IR. The observation that ghrelin and BIM-28163 have different efficacies in inducing Fos-IR in the DMH, and that concomitant administration of ghrelin and an excess of BIM-28163 results in the same level of Fos-IR as BIM-28163 administered alone may demonstrate that in the DMH both ghrelin and BIM-28163 act via the same receptor. If so, it is unlikely that this receptor is GHS-1a. Collectively, our findings suggest that the action of ghrelin to stimulate increased weight gain may be mediated by a novel receptor other than GHS-1a, and further imply that GHS-1a may not be the appropriate target for anti-obesity strategies.
CC 2-5 (Mammalian Hormones)
IT Body weight
(gain; GHS-1a receptor antagonist blocks ghrelin-induced growth hormone secretion but induces increased body weight gain)
IT 258279-04-8, Human Ghrelin 304853-26-7D, Ghrelin, analog
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GHS-1a receptor antagonist blocks ghrelin-induced growth hormone secretion but induces increased body weight gain)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 48 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:305176 CAPLUS Full-text
DOCUMENT NUMBER: 143:131584
TITLE: Evaluation of blood active ghrelin and adipocytokines in patients with inflammatory bowel disease and liver cirrhosis
AUTHOR(S): Oriishi, Tetsuharu; Itou, Minoru; Toyonaga, Atsushi; Sata, Michio
CORPORATE SOURCE: The Second Department of Internal Medicine, Kurume University School of Medicine, Japan
SOURCE: Shoka to Kyushu (2005), Volume Date 2004, 27(1), 39-43
CODEN: SHKYEZ; ISSN: 0389-3626
PUBLISHER: Nippon Shoka Kyushu Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB We evaluated blood active ghrelin, desacyl-ghrelin, leptin and adiponectin in patients with inflammatory bowel disease and liver cirrhosis. Subjects were 12 patients with Crohn's disease (CD), 17 patients with ulcerative colitis (UC), 14 patients with liver cirrhosis (LC), 10 elders, over 80 years old, and 8 healthy controls. We obtained blood sample in fasting morning and measured 16 times in patients with CD, 7 times in active phase and 9 times in inactive

phase, 22 times in patients with UC, 10 times in active phase and 12 times in remission. Blood level of active ghrelin was significantly higher in CD than in controls, significantly lower in LC and in elders than in controls, although blood level of desacyl-ghrelin was not significantly different in any subject group compared with controls. Blood level of leptin was lower in CD than in controls and adiponectin was higher in LC than in controls. Score of BMI in CD and in elders was lower than in controls, and blood level of albumin, total cholesterol and BCAA was lower in LC and in CD than in controls. Changing pattern of blood level of active ghrelin, desacyl-ghrelin, leptin, and adiponectin in each subject group compared with controls was different resp. Nutritional assessment was lower and active ghrelin was higher in active CD than in inactive CD, though no difference was seen between in active UC and in remission UC. These suggesting that mechanism of malnutrition is differ in each subject group resp. and measuring blood active ghrelin is useful for assessment of malnutrition.
CC 15-8 (Immunochemistry)
Section cross-reference(s): 14
IT Blood
Cirrhosis
Human
Malnutrition
(evaluation of blood active ghrelin and adipocytokines in patients with inflammatory bowel disease and liver cirrhosis)
IT 57-88-5, Cholesterol, biological studies 169494-85-3, Leptin 304853-26-7, Ghrelin 304853-26-7D, Ghrelin, desacylated
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(evaluation of blood active ghrelin and adipocytokines in patients with inflammatory bowel disease and liver cirrhosis)

L99 ANSWER 49 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:59342 CAPLUS Full-text
DOCUMENT NUMBER: 142:233444
TITLE: Separate measurement of plasma levels of acylated and desacyl ghrelin in healthy subjects using a new direct ELISA assay
AUTHOR(S): Akamizu, Takashi; Shinomiya, Toshiaki; Irako, Taiga; Fukunaga, Mikihiko; Nakai, Yoshihide; Nakai, Yoshikatsu; Kangawa, Kenji
CORPORATE SOURCE: Ghrelin Research Project, Department of Experimental Therapeutics, Translational Research Center, Kyoto University Hospital, Faculty of Medicine, Kyoto University, Kyoto, 606-8507, Japan
SOURCE: Journal of Clinical Endocrinology and Metabolism (2005), 90(1), 6-9
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two forms of ghrelin, acylated and desacyl, circulate in plasma. Although acylation is thought to be essential for ghrelin biol. activities, recent studies have suggested that desacyl ghrelin may also possess biol. activity. A new com. ELISA system has now enabled us to measure plasma levels of each of these two ghrelin forms sep. This assay system directly measures levels using small amts. of plasma. To evaluate the utility of this assay system, we measured the plasma levels of the two forms of ghrelin in healthy volunteers. Although acylated ghrelin levels were equivalent to those measured previously by RIA, desacyl ghrelin levels were lower than those expected from the total ghrelin levels previously determined by RIA. The ratios of acylated to desacyl ghrelin significantly correlated with previously determined acylated, but not desacyl, ghrelin levels. After BMI adjustment, the levels of

acylated, but not desacyl, ghrelin plasma levels were higher in female subjects than those in males. Several metabolic and hormonal parameters significantly correlated with either plasma acylated or desacyl ghrelin levels. These findings indicate that sep. measurements of the two ghrelin form levels may provide valuable information on their structure, gender differences, and physiol. implications.

CC 2-1 (Mammalian Hormones)

IT Blood analysis
Body weight
Human
(sep. measurement of plasma levels of acylated and desacyl ghrelin in healthy subjects using a new direct ELISA assay and correlation with hormonal and metabolic parameters)

IT 304853-26-7, Ghrelin 304853-26-7D, Ghrelin, desacyl
RL: ANT (Analyte); ANST (Analytical study)
(sep. measurement of plasma levels of acylated and desacyl ghrelin in healthy subjects using a new direct ELISA assay and correlation with hormonal and metabolic parameters)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 50 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:491064 CAPLUS Full-text
DOCUMENT NUMBER: 139:47174
TITLE: Pharmaceutical compositions comprising unacylated ghrelin and therapeutical uses for metabolic disorders
INVENTOR(S): Ghigo, Ezio; Van der Lely, Aart Jan
PATENT ASSIGNEE(S): Theratechnologies Inc., Can.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051389	A2	20030626	WO 2002-CA1964	20021218
WO 2003051389	A3	20030912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2470235	A1	20030626	CA 2002-2470235	20021218
AU 2002351593	A1	20030630	AU 2002-351593	20021218
EP 1455814	A2	20040915	EP 2002-787266	20021218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2005080007	A1	20050414	US 2003-499376	20021218
JP 2005511771	T	20050428	JP 2003-552322	20021218
PRIORITY APPLN. INFO.:			CA 2001-2365704 A	20011218
			WO 2002-CA1964 W	20021218

AB The present invention relates to compns. containing unacetylaed ghrelin and derivs. thereof and their uses in the control of glycemia in ageing patients, GH deficient patients, diabetic patients and obese patients.

IC ICM A61K038-22
ICS A61P003-04; A61P003-10

CC 1-10 (Pharmacology)
Section cross-reference(s): 63

IT Body weight
(controlling of; pharmaceutical compns. comprising unacylated ghrelin and therapeutical uses for metabolic disorders)

IT 304853-26-7D, Ghrelin, deacylation products
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. comprising unacylated ghrelin and therapeutical uses for metabolic disorders)

L99 ANSWER 51 OF 66 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:581723 CAPLUS Full-text
DOCUMENT NUMBER: 135:147451
TITLE: Use of compounds for the regulation of food intake
INVENTOR(S): Andersen, Maibritt Bansholm; Hansen, Birgit Sehested; Raun, Kirsten; Tullin, Soren; Thim, Lars
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001056592	A1	20010809	WO 2001-DK64	20010129
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			DK 2000-161 A	20000201
			DK 2000-1107 A	20000717

AB Compds. that are ligands for the receptor GHS-R 1A, as well as pharmaceutically acceptable salts thereof, are useful for the manufacture of medicaments for the regulation of food intake.

IC ICM A61K038-17
ICS A61K031-7076; A61P003-04

CC 1-11 (Pharmacology)
Section cross-reference(s): 2

ST appetite regulation growth hormone secretagogue receptor ligand

IT AIDS (disease)
(body wasting in, treatment of; use of compds. for regulation of food intake that are ligands of growth hormone secretagogue type 1A receptors (GHS-R 1A) in relation to growth hormone release)

IT Body weight
(regulation of; use of compds. for regulation of food intake that are ligands of growth hormone secretagogue type 1A receptors (GHS-R 1A) in relation to growth hormone release)

IT Antidiabetic agents
Antiobesity agents
Appetite
Appetite depressants
Drug delivery systems
Drug screening
Feeding
(use of compds. for regulation of food intake that are ligands of growth hormone secretagogue type 1A receptors (GHS-R 1A) in relation to growth hormone release)
IT Disease, animal
(wasting, in AIDS, treatment of; use of compds. for regulation of food intake that are ligands of growth hormone secretagogue type 1A receptors (GHS-R 1A) in relation to growth hormone release)
IT 9002-72-6, Somatotropin
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(deficiency and secretion of, stimulation of appetite in relation to; use of compds. for regulation of food intake that are ligands of growth hormone secretagogue type 1A receptors (GHS-R 1A) in relation to growth hormone release)
IT 58-61-7, Adenosine, biological studies 193079-69-5, NN703 267225-30-9, NNC 26-1187 304853-26-7, Ghrelin 304853-26-7D, Ghrelin, homologs 353289-95-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of compds. for regulation of food intake that are ligands of growth hormone secretagogue type 1A receptors (GHS-R 1A) in relation to growth hormone release)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 52 OF 66 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2007-476486 [46] WPIX
DOC. NO. CPI: C2007-173901 [46]
DOC. NO. NON-CPI: N2007-362182 [46]
TITLE: New ghrelin peptidyl analogs useful for e. g. stimulating growth hormone secretion, treating growth hormone deficient state, increasing muscle mass and bone density, treating sexual dysfunction
DERWENT CLASS: B04; S03
INVENTOR: COMSTOCK J M; CULLER M D; DONG Z X; SHEN Y
PATENT ASSIGNEE: (SCRC-C) SAS SOC CONSEILS RECH & APPL SCI; (COMS-I) COMSTOCK J M; (CULL-I) CULLER M D; (DONG-I) DONG Z X; (SHEN-I) SHEN Y
COUNTRY COUNT: 115

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2007038678	A2	20070405	(200746)*	EN	110[0]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2007038678 A2		WO 2006-US37889	20060927

PRIORITY APPLN. INFO: US 2005-750771P 20051215
US 2005-721557P 20050928
US 2005-748904P 20051209
INT. PATENT CLASSIF.:
IPC ORIGINAL: A61K0038-22 [I,A]; A61K0038-22 [I,C]
BASIC ABSTRACT:
WO 2007038678 A2 UPAB: 20070719
NOVELTY - Ghrelin peptidyl analogs, or their salts are new.
DETAILED DESCRIPTION - Ghrelin peptidyl analogs of formula (R2R3)-A1-A2-A3-A4-A5-A6-A7-A8-A9-A10-A11-A12-A13-A14-A15-A16- A17-A18-A19-A20-A21-A22-A23-A24-A25-A26-A27-A28-R1, or their salts are new.
A1=e.g. Gly or Aib;
A2=e.g. Ser, Aib, Ava;
A3=e.g. Asp(NH-hexyl), Asp(1-heptanol), Cys(S-(CH2)9CH3), Glu(NH-hexyl) or Glu(1-heptanol);
A4=e.g. Phe;
A5=e.g. Leu;
A6=e.g. Ser;
A7=e.g. Pro, Dhp (3,4-dehydroproline), 4-Hyp (4-hydroxyproline), Pip (pipecolic acid), Thz (thiazolidine-4-carboxylic acid) or Tic (1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid); A8=e.g. Glu or Aib;
A9=e.g. His, 3-Pal (beta-(3-pyridinyl)alanine), 4-Pal (beta-(4-pyridinyl)alanine), Taz (beta-(4-thiazolyl)alanine)or 2-Thi (beta-(2-thienyl)alanine);
A10=e.g. Gln or Aib;
A11=e.g. Arg;
A12=e.g. Val;
A13 and A14=e.g. Gln;
A15=e.g. Arg, Glu(NH-hexyl) or Ser(n-octanoyl); A16=e.g. Lys, Glu(NH-hexyl) or Ser(n-octanoyl); A17=e.g. Glu, Lys(biotinyl), Asp(NH-hexyl), Asp(1-heptanol), CyS(S-(CH2)9CH3), Dap(octanesulfonyl), Glu-(NH-hexyl), Glu(1-heptanol) or Ser(n-octanoyl);
A18=e.g. Ser, Glu(NH-hexyl) or Ser(n-octanoyl); A19 and A20=e.g. Lys, Glu(NH-hexyl) or Ser(n-octanoyl); A21, A22 and A27=e.g. Pro;
A23=e.g. Ala;
A24= e.g. Lys;
A25=e.g. Leu;
A26=e.g. Gln;
A28=e.g. Arg;and
R2 and R3=e.g. H, 1-6C acyl, n-butyryl, isobutyryl or n-octanoyl. Full Definitions are given in the DEFINITIONS (Full Definitions) Section. An INDEPENDENT CLAIM is included for screening for a compound able to bind to a GHS (growth hormone secretagogue) receptor involving measuring the ability of a compound to affect binding of (I) to the receptor, to a fragment of the receptor, to a polypeptide comprising the fragment of the receptor, or to a derivative of the polypeptide. ACTIVITY - Endocrine-Gen.; Muscular-Gen.; Osteopathic; Anorectic; Gastrointestinal-Gen.; Respiratory-Gen.; Antidiabetic; Ophthalmological; Cardiovascular-Gen.; Antiinflammatory; Antiasthmatic; Antiarthritic; Hepatotropic; Immunosuppressive; Neuroprotective; Nootropic; Dermatological; Antirheumatic; Vasotropic; Antiallergic; Antipsoriatic; Antiulcer; Anabolic; Hypertensive; Antithyroid.
MECHANISM OF ACTION - Ghrelin modulator; Growth hormone (GH) secretagogue receptor modulator. The GHS-R (growth hormone secretagogue receptor) binding activity of (Lys(biotinyl)17)hghrelin(1 - 28)-NH2 (IA) was tested as follows. Membranes for radioligand binding studies were prepared by homogenization of

CHO-K1 cells expressing the human recombinant GHS receptor. The homogenates were washed twice by centrifugation (39000 g/10 minutes) and the final pellets were resuspended in 50 mM Tris-HCl containing 2.5 mM MgCl2 and 0.1% bovine serum albumin (BSA). For the selected assay, aliquots of approximately0.4 ml were incubated with 0.05 nM (125I)ghrelin (2000 Ci/mmol) with and without 0.05 ml of unlabeled competing test peptide. After approximately60 minutes at 4degreesC, the bound (125I)ghrelin was separated from the free ghrelin by rapid filtration which were pre-soaked in 0.5% polyethyleneimine/0.1% BSA. The filters were then washed 3 times with 5-ml aliquots of ice-cold 50 mM Tris-HCl and 0.1% BSA. (IA) Showed a Ki value of 0.07 nM.

USE - For stimulating growth hormone secretion in a subject; for treating growth hormone deficient state, for increasing muscle mass and bone density, for treating sexual dysfunction in males or females, for facilitating a weight gain, for facilitating maintenance of weight, physical functioning, recovery of physical function and/or appetite increase; for treating weight loss associated with the onset of cachexia (where the cachexia is incidental to the subject suffering from anorexia, bulimia, cancer, AIDS or chronic obstructive pulmonary disease), weight loss due to the onset of wasting syndrome, particularly in the frail or elderly, onset of Alzheimer's diseases, due to chemotherapy, radiation therapy, temporary immobilization, permanent immobilization and dialysis; for treating or preventing post-operative ileus or chronic obstructive pulmonary diseases; for treating disease caused by excessive growth hormone secretion (where the excessive weight gain is a contributing factor of diseases e.g. hypertension, dyslipidemia, gall stones, osteoarthritis and cancers, Prader-Willi syndrome), for facilitation of loss of excessive body weight, for facilitation of appetite decrease and weight maintenance, for treating obesity, diabetes, complications of diabetes including retinopathy, and/or cardiovascular disorders; for treating inflammation in a subject; for treating inflammation associated with infectious process such as viral infection e.g. hepatitis A virus, human immunodeficiency virus; bacterial infection e.g. Staphylococcus aureus; parasitic infection, fungal infection; inflammation associated with liver-toxicity (where the liver toxicity is associated with caner therapy e.g. apoptosis induction and/or chemotherapy), transplant rejection, burn, lung inflammation, and cancer; for treating loss of appetite caused by inflammation (low grade inflammation caused by aging); for treating inflammatory diseases (e.g. asthma, reactive arthritis, hepatitis, spondyarthritis, Sjogren's syndrome, Alzheimer's disease and atopic dermatitis), autoimmune disease (e.g. systemic lupus erythematosus, rheumatoid arthritis, systemic vasculitis, insulin dependent diabetes mellitus, multiple sclerosis, muscular dystrophy, experimental allergic encephalomyelitis, psoriasis, Crohn's disease, inflammatory bowel disease, ulcerative colitis, Addison's disease, alopecia areata, celiac disease, thyroid disease, scleroderma) (claimed).

ADVANTAGE - The peptidyl analogs possess agonist or antagonist ghrelin activity, and it exhibits higher cell membrane binding affinity and is found to interact more efficiently with membrane bound receptors and thus are more biologically potent compared to native ghrelin. It achieves a beneficial affect in a subject by helping to cure or reduce the severity or reduces the likelihood of onset or severity a disease or disorder. It stimulates or suppresses growth hormone secretion in a subject.

MANUAL CODE: CPI: B04-J01; B11-C08E; B12-K04E1; B14-C03; B14-C09; B14-D01; B14-E08; B14-E10C; B14-E11; B14-E12; B14-F01; B14-F02; B14-G02; B14-H01; B14-J01A4; B14-J05; B14-K01; B14-N01; B14-N03; B14-N11; B14-N12; B14-N17; B14-P04; B14-R02; B14-S01; B14-S04; B14-S16
EPI: S03-E04E; S03-E14A1

TECH

ORGANIC CHEMISTRY - Preparation (disclosed): No general methods for the preparation of ghrelin peptidyl analogs (I) are given.

L99 ANSWER 53 OF 66 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2007-283319 [27] WPIX
DOC. NO. CPI: C2007-103794 [27]
TITLE: New peptide or peptidomimetic compounds, useful for treating diseases such as anorexia, arthritis, inflammatory bowel disease, ulcerative colitis, obesity, hypertension, diabetes, and AIDS
DERWENT CLASS: B02; B04
INVENTOR: DONG Z X; EYNON J S; SHEN Y
PATENT ASSIGNEE: (SCRC-C) SAS SOC CONSEILS RECH & APPL SCI; (DONG-I) DONG Z X; (EYNO-I) EYNON J S; (SHEN-I) SHEN Y
COUNTRY COUNT: 113

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2007014258	A2	20070201	(200727)*	EN	171[0]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2007014258	A2	WO 2006-US29002	20060724

PRIORITY APPLN. INFO: US 2005-701729P 20050722
INT. PATENT CLASSIF.:
IPC ORIGINAL: C07K0014-435 [I,C]; C07K0014-60 [I,A]; C12P0021-06 [I,A]; C12P0021-06 [I,C]

BASIC ABSTRACT:

WO 2007014258 A2 UPAB: 20070426

NOVELTY - Peptide or peptidomimetic compounds (I) or (II) and their salts are new.

DETAILED DESCRIPTION - Peptide or peptidomimetic compounds of formula (I) or (II), and their salts are new. X= a group of formula (Xa), (Xb), or (Xc); Y=H or NR12N13;
Z=C(O)- or -SO2-;
n=1-8;
R1, R3=H or 1-4C alkyl;
R2, R4=indene or naphthalene-containing radical; R5=H, optionally substituted (1-6C alkyl, 2-6C alkenyl, or 2-6C alkynyl), aryl, alkylaryl, alkylarylalkyl, or arylalkylaryl; R6, R9=optionally substituted 1-6C alkyl; R6, R7, R10-R13=H, or optionally substituted 1-6C alkyl. Provided that R2 and R4 are not radical of formula (Xd), where Q is H or 1-4C alkyl.

INDEPENDENT CLAIMS are also included for the following: (1) determining an ability of the compound to bind to growth hormone secretagogues (GHS), comprising measuring the ability of the compound to effect binding with receptor, fragment of receptor, polypeptide of the receptor fragment, or derivative of the polypeptide; (2) screening for a ghrelin agonist, comprising using the inventive compound or its salt in a competition experiment with test compounds;
(3) screening for a ghrelin antagonist, comprising using the inventive compound or its salt to produce GHS receptor activity and then measuring the ability of a test compound to alter GHS receptor activity; (4) achieving a beneficial effect in a subject, comprising administering to the subject the inventive compound or its salt to a patient;
(5) stimulating growth hormone secretion in a subject, comprising administering to a subject a ghrelin agonist or its salt in an amount effective to produce a detectable increase in growth hormone secretion; (6) suppressing growth hormone secretion in a subject, comprising administering to

a subject a ghrelin antagonist of formula (I) or (II) or its salt in an amount that is sufficient to produce a detectable decrease in growth hormone secretion;
(7) eliciting a ghrelin agonist or antagonist effect in a subject, comprising administering to a subject a ghrelin agonist or antagonist of formula (I) or (II) or its salt in an amount sufficient to produce a detectable decrease in growth hormone secretion; and (8) promoting gastrointestinal motility in a subject, comprising administering to a subject a ghrelin antagonist of formula (I) or (II) or its salt in an amount that is sufficient to facilitate gastrointestinal motility.
ACTIVITY - Anabolic; Eating-Disorders-Gen; Cytostatic; Anti-HIV; Anabolic; Cardiovascular-Gen.; Osteopathic; Antiarthritic; Antiinflammatory; Dermatological; Immunosuppressive; Gastrointestinal- Gen.; Antiulcer; Anorectic; Hypotensive; Antidiabetic; Antilipemic.
MECHANISM OF ACTION - Ghrelin agonist; Ghrelin antagonist. Growth hormone release stimulator; Growth hormone release stimulator. (I) and (II) were tested for their ability to stimulate release of growth hormone. The compound was injected subcutaneously in 10-day old rats at a dose of 300 mg/kg. After 15 minutes, the growth hormone levels were measured and compared to growth hormone levels in rats injected with solvent control. No results are given.
USE - As ghrelin agonists for stimulating growth hormone secretion in a subject having disease or disorder accompanied by weight loss. As ghrelin antagonists for suppressing growth hormone in a subject having disease or condition characterized by excessive weight. For promoting gastrointestinal mobility in a subject suffering from post-operative gastroparesis (which is incidental to the onset of diabetes or is brought about by chronic diabetic state). Also in screening for a ghrelin agonist or antagonist. The diseases or disorders accompanied by weight loss include anorexia, bulimia, cancer cachexia, AIDS, AIDS wasting, cachexia, cardiovascular disease, osteoporosis, arthritis, systemic lupus erythematosus, inflammatory bowel disease, Crohn's Disease, ulcerative colitis, chronic renal failure, or wasting in frail elderly. The excessive weight is especially a contributing factor to a disease or condition including obesity, hypertension, diabetes, dyslipidemia, cardiovascular disease, gall stones, osteoarthritis, Prader-Willi Syndrome and cancer (all claimed). As functional ghrelin analogs both as research tool and/or as therapeutic agents. Also useful in e.g. screening for compounds active at the GHS receptor, for determining the presence of GHS receptor in a sample, or in preparing and examining the role or effect of ghrelin.
ADVANTAGE - The inventive compound is active at GS receptor. It is capable of binding to the receptor and MANUAL CODE: CPI: B06-B01; B06-D01; B07-D05; B10-A08; B10-A09B;

B10-B01B; B10-B02F; B11-C08E2; B12-K04E; B12-K04E1; B14-A02B1; B14-C09; B14-D02A2; B14-E08; B14-E10; B14-E11; B14-E12; B14-F01; B14-F02; B14-F06A; B14-G01B; B14-G02D; B14-H01; B14-J05; B14-L01; B14-L06; B14-N01A; B14-N10; B14-N12; B14-N17; B14-S04; B14-S16; B14-S20A

TECH
ORGANIC CHEMISTRY - Preparation: (I) and (II) are prepared by treating an intermediate containing indole and tert-butyl oxycarbonyl with a solution containing trifluoroacetic acid, evaporating the solution, triturating by adding cold ether to the residue and collecting the precipitate, and purifying the formed crude product.
Preferred Method: The stimulation of growth hormone secretion is indicated for treatment of a growth hormone deficient state, for increasing muscle mass, for increasing bone density, for sexual dysfunction in males or females, for facilitating a weight gain, for facilitating maintenance of weight for facilitating maintenance of physical functioning, for facilitating recovery of physical function, and/or facilitating appetite increase. The treatment for growth hormone deficient state includes chemotherapy, radiation therapy, temporary or permanent immobilization,

and dialysis. The suppression of growth hormone secretion is indicated for the treatment of disease or condition characterized by excessive growth hormone secretion, for facilitation of weight loss, for facilitation of appetite decrease, for facilitation of weight maintenance, for treating obesity, for treating diabetes, for treating complications of diabetes including retinopathy, and/or for treating cardiovascular disorders.

L99 ANSWER 54 OF 66 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-100672 [11] WPIX
DOC. NO. CPI: C2005-033673 [11]
TITLE: New tetraline derivatives useful for the treatment of disorders regulated by ghrelin e.g. anorexia, cancer cachexia, eating disorders, age-related decline in body composition, weight gain, obesity and diabetes mellitus
DERWENT CLASS: B03; B05
INVENTOR: LIU B; LIU G; NELSON L T J; PATEL J R; SHAM H L; XIN Z; ZHAO H
PATENT ASSIGNEE: (LIUB-I) LIU B; (LIUG-I) LIU G; (NELS-I) NELSON L T J; (PATE-I) PATEL J R; (SHAM-I) SHAM H L; (XINZ-I) XIN Z; (ZHAO-I) ZHAO H; (ABBO-C) ABBOTT LAB
COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND DATE	WEEK	LA	PG	MAIN IPC
US 20050014794	A1 20050120 (200511)*	EN		35[0]	
US 7115767	B2 20061003 (200665)	EN			

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20050014794	A1 Provisional	US 2003-488250P	20030718
US 20050014794	A1	US 2004-893484	20040716

PRIORITY APPLN. INFO: US 2004-893484 20040716
US 2003-488250P 20030718
INT. PATENT CLASSIF.:
IPC ORIGINAL: A61K0031-21 [I,C]; A61K0031-27 [I,A]; C07C0271-00 [I,C]; C07C0271-06 [I,A]
IPC RECLASSIF.: A61K0031-165 [I,A]; A61K0031-165 [I,C]; A61K0031-185 [I,C]; A61K0031-195 [I,A]; A61K0031-275 [I,C]; A61K0031-277 [I,A]; A61K0031-401 [I,A]; A61K0031-401 [I,C]; A61K0031-445 [I,A]; A61K0031-445 [I,C]; C07D0211-00 [I,C]; C07D0211-06 [I,A]
BASIC ABSTRACT:
US 20050014794 A1 UPAB: 20050708
NOVELTY - Tetraline derivatives (I-II) are new.
DETAILED DESCRIPTION - Tetraline derivatives of formula (I-II) and their salts and derivatives are new. R1,R2 = H, alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle or heterocyclealkyl; N(R1+R2) = heterocycle;
R3-R6 = H, alkoxy, alkoxyalkyl, alkyl, alkenyl, alkenylalkoxy, aryl, cyano, cycloalkyl, (halo)alkyl, heterocycle, (hydroxy)alkyl, nitro, sulfonyl, RaRbN-, RaRbN-alkyl, RaRbN-carboxyalkyl, RaRbN-carboxyalkenyl or RaRbN-sulfonyl;
R7 = H, alkenyl, alkyl, (alkoxy)carbonyl, aryl, hydroxy, haloalkyl, cycloalkyl, heterocycle, RcRdN-, RcRdN-carboxy or RcRdN-sulfonyl;

R8-R13 = H, (alkoxy)alkyl, alkyl, (alkenyl)alkoxy, aryl, cyano, (halo)alkyl, heterocycle, (hydroxy)alkyl, RaRbN-, RaRbN-alkyl or RaRbN-carboxyalkyl; R14 = undefined; Ra,Rb = H, alkenyloxycarbonyl, alkoxyalkyl, (alkyl)carbonyl, alkoxycarbonyl, alkoxycarbonylalkylalkoxyalkoxycarbonyl, alkylsulfonyl, alkynyloxycarbonyl, (aryl)alkyl, arylalkoxycarbonyl, aryloxyalkyl, aryloxyalkylcarbonyl, cycloalkyl, cycloalkoxycarbonyl, cycloalkylalkyl, cycloalkylalkoxycarbonyl, heterocycle, heterocyclecarbonyl, heterocyclealkyl, heterocyclealkoxyl carbonyl, hydroxyalkoxycarbonyl, haloalkoxycarbonyl, RcRdN-carbonyl, RcRdN-carbonylalkyl-, RcRdN-alkyl, or RcRdN-alkoxycarbonyl; Rc,Rd = H, alkenyloxycarbonyl, alkoxyalkyl, alkyl, alkylcarbonyl, alkylNHalkylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkoxyalkoxycarbonyl, alkylsulfonyl, alkynyloxycarbonyl, (aryl)alkyl, arylalkoxycarbonyl, aryloxyalkyl, aryloxyalkylcarbonyl, cycloalkyl; cycloalkoxycarbonyl, cycloalkylalkyl, cycloalkylalkoxycarbonyl, heterocycle, heterocyclecarbonyl, heterocyclealkyl, heterocyclealkoxyl carbonyl, hydroxyalkoxycarbonyl, haloalkoxycarbonyl, nitroalkoxycarbonyl, ReRfN-carbonyl, ReRfN-carbonylalkyl, ReRfN-alkyl; or ReRfN-alkoxycarbonyl; Re,Rf = H or alkyl.

ACTIVITY - Anabolic; Cytostatic; Immunomodulator; Eating Disorders Gen.; Anorectic; Antidiabetic.

MECHANISM OF ACTION - Ghrelin receptor modulators. Test details are described but no results for specific compounds are given. In general the tetraline compounds show an IC50 value of 0.001 - 0.2 microM.

USE - In the preparation of a composition useful for the treatment of anorexia, cancer cachexia, eating disorders, age-related decline in body composition, weight gain, obesity and diabetes mellitus (Claimed).

ADVANTAGE - The tetraline derivatives modulate ghrelin receptors.

MANUAL CODE: CPI: B06-H; B07-H; B10-B02B; B14-E11A; B14-E11B ; B14-E12; B14-S04A

TECH

ORGANIC CHEMISTRY - Preparation: The tetraline derivative (I) (in which R7 is NH-C(O)-O-CH2-C(CH3)2) is prepared by treating a compound of formula (i) with sodium iodide and methyl iodide in dimethylformamide to form a compound of formula (ii), treating (ii) with lithium diisopropylamine in tetrahydrofuran followed by treatment with di-tert-butyl dicarbonate to form a compound of formula (iii), hydrolyzing (iii) with lithium hydroxide, sodium hydroxide in aqueous methanol to form (iv), treating (iv) with diphenoxyphosphonium azide and triethyl amine in a mixture of tetrahydrofuran and iso-butyl alcohol under heated conditions to form a compound of formula (v), treating (v) with 4 N hydrochloric acid in dioxane or trifluoroacetic acid in dichloromethane to form a compound of formula (vi) and reacting (vi) with an amine of formula R1R2NH in the presence of (benzotriazol-1-yloxy)-dimethylamino-methylene)-dimethyl-ammonium tetrafluoroborate (TBTU) and triethylamine in dimethylformamide.

L99 ANSWER 55 OF 66 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-195531 [25] WPIX

DOC. NO. CPI: C2002-060339 [25]

TITLE: Truncated ghrelin analogs active at growth-hormone secretagogue receptor useful for diagnosing or treating diseases such as anorexia, bulimia, cancer, obesity, diabetes mellitus, hypertension, osteoarthritis

DERWENT CLASS: B04; D16

INVENTOR: BEDNAREK M; BEDNAREK M A

PATENT ASSIGNEE: (BEDN-I) BEDNAREK M A; (MERI-C) MERCK & CO INC

COUNTRY COUNT: 23

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001092292	A2	20011206	(200225)*	EN	37[0]	
US 20030186844	A1	20031002	(200365)	EN		
EP 1353683	A2	20031022	(200370)	EN		
JP 2004514651	W	20040520	(200434)	JA	64	
US 6967237	B2	20051122	(200577)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001092292	A2	WO 2001-US17026	20010525
US 6967237	B2 Provisional	US 2000-207920P	20000530
EP 1353683	A2	EP 2001-939465	20010525
US 20030186844	A1	WO 2001-US17026	20010525
EP 1353683	A2	WO 2001-US17026	20010525
JP 2004514651	W	WO 2001-US17026	20010525
US 6967237	B2	WO 2001-US17026	20010525
JP 2004514651	W	JP 2002-500904	20010525
US 20030186844	A1	US 2002-276392	20021115
US 6967237	B2	US 2002-276392	20021115

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1353683	A2 Based on	WO 2001092292 A
JP 2004514651	W Based on	WO 2001092292 A
US 6967237	B2 Based on	WO 2001092292 A

PRIORITY APPLN. INFO: US 2000-207920P 20000530
US 2002-276392 20021115

INT. PATENT CLASSIF.:

MAIN: C07K005-08

IPC RECLASSIF.: A61K0038-00 [I,A]; A61K0038-00 [I,C]; A61K0038-25 [I,A]; A61K0038-25 [I,C]; A61K0038-27 [I,A]; A61K0038-27 [I,C]; A61P0043-00 [I,A]; A61P0043-00 [I,C]; A61P0005-00 [I,C]; A61P0005-06 [I,A]; C07K0014-435 [I,C]; C07K0014-47 [I,A]; C07K0014-60 [I,A]; C07K0005-00 [I,C]; C07K0005-08 [I,A]; C07K0005-10 [I,A]; C07K0005-103 [I,A]; C07K0007-00 [I,C]; C07K0007-04 [I,A]; C12N0015-09 [I,A]; C12N0015-09 [I,C]

BASIC ABSTRACT:

WO 2001092292 A2 UPAB: 20060202

NOVELTY - A truncated ghrelin analog (I) having a structure (A) or (B) or their salt, active at growth-hormone secretagogue (GHS) receptor, is new.

DETAILED DESCRIPTION - (I) has a structure (A) or (B) Z1-GSXF(Z)n-Z2 (A) Z1-GXSF(Z)n-Z2 (B), where X = modified amino acid containing a bulky hydrophobic R group; Z = A, V, L, I, P, W, F, M, G, S, T, Y, C, N, Q, K, R, H, D, E, or their derivatives; Z1 = an optionally present protecting group, if present is covalently joined to N-terminal amino group; Z2 = an optionally present protecting group, if present is covalently joined to C-terminal amino group; and n = 0-19. ACTIVITY - Cytostatic; Metabolic; Immunomodulator; Anti-human immunodeficiency virus (HIV); Anorectic; Antidiabetic; Ophthalmological; Hypotensive; Antilipemic; Cardiant; Osteopathic; Antiarthritic; Litholytic; Hepatotropic.

MECHANISM OF ACTION - Ghrelin agonist or antagonist.

USE - (I) is useful for screening a compound capable of binding to GHS receptor. The method comprises measuring the ability of the compound to effect

the binding of (I) to either the receptor, a fragment of the receptor comprising ghrelin binding site, a polypeptide comprising the fragment or derivative of the polypeptide, where the ability of the analog to bind the receptor is measured. (I) is also useful for achieving a beneficial effect in a subject; and for stimulating growth hormone secretion (claimed). (I) is useful as a research tool which include determining the presence of GHS receptor in a sample or preparation, and examining the role of effect of ghrelin. (I) is further useful for screening both agonist and antagonist of ghrelin, which are used therapeutically, where ghrelin agonist is utilized for treating a growth hormone deficient state, increasing muscle mass and bone density, treating sexual dysfunction in males or females, facilitating a weight gain, maintenance of weight, maintenance of physical functioning, recovery of physical function, and/or appetite increase, where a weight gain, maintenance in weight, or appetite increase is particularly useful for a patient having a disease or disorder, or under going a treatment, accompanied by weight loss such as anorexia, bulimia, cancer cachexia, acquired immunodeficiency syndrome (AIDS), wasting, cachexia, and wasting in frail elderly, and examples of treatments accompanied by weight loss include chemotherapy, radiation therapy, temporary or permanent immobilization, and dialysis; and ghrelin antagonist is utilized to facilitate weight loss, appetite decrease, weight maintenance, treat obesity, diabetes, and complications of diabetes including retinopathy, and/or cardiovascular disorders, where excessive weight is a contributing factor to different diseases including hypertension, diabetes, dyslipidemias, cardiovascular disease, gall stones, osteoarthritis and certain forms of cancers, and bringing about a weight loss can be used, for e.g. to reduce the likelihood of such diseases and for treating such diseases.

ADVANTAGE - (I) induces growth hormone release from primary-culture pituitary cells in a dose-dependent manner without stimulating the release of other pituitary hormones. Unlike longer length ghrelin, (I) can be synthesized easily and has increased solubility in physiological buffers.

MANUAL CODE: CPI: B04-C01; B04-C01F; B14-A02; B14-A02B1; B14-C09; B14-E12; B14-F01; B14-F02; B14-F06; B14-G03; B14-H01; B14-L06; B14-N01; B14-N03; B14-N12; B14-S04; D05-C12; D05-H17A5; D05-H18

TECH

BIOTECHNOLOGY - Preparation: (I) is prepared by standard biochemical synthesis involving introduction of nucleic acid into a cell and expression of the nucleic acids. Preferred Analog: In structure (A) or (B), X has a structure (C); where X1 = -O-, -S-, -OC(O)-, -NHC(O)-, or -CH2-; and R = -C(4-20) alkyl, -C(4-20) substituted alkyl, -C(4-20) substituted alkenyl, -C(4-20) alkenyl, -C(4-20) heteroalkyl, -C(4-20) substituted heteroalkyl, aryl, or alkylaryl. Preferably the structure of (I) is (A), where N = 0-11 preferably 0-6 or 0-3 and more preferably 0, and X1 = -C(O)- or -NH(O)-, and R = -C(5-15) alkyl more preferably -(CH2)6CH3, where Z1 (if present) = -C(O)CH3 and Z2 (if present) = -NH2.

ORGANIC CHEMISTRY - Preparation: (I) is synthesized by standard chemical synthesis e.g. Vincent in Peptide and Protein Drug Delivery, New York, N.Y., Dekker, 1990.

L99 ANSWER 56 OF 66 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2007059803 EMBASE Full-text
TITLE: Cancer cachexia: It's time for more clinical trials.
AUTHOR: Bossola M.; Pacelli F.; Tortorelli A.; Doglietto G.B.
CORPORATE SOURCE: M. Bossola, Istituto di Clinica Chirurgica, Universita Cattolica del Sacro Cuore, Largo A. Gemelli, 8, 00168,

Roma, Italy. maubosso@tin.it
SOURCE: Annals of Surgical Oncology, (2007) Vol. 14, No. 2, pp. 276-285. .
Refs: 84
ISSN: 1068-9265 E-ISSN: 1534-4681 CODEN: ASONF4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
005 General Pathology and Pathological Anatomy
009 Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Feb 2007
Last Updated on STN: 16 Feb 2007

ABSTRACT: Cancer cachexia (CC) is a multifactorial paraneoplastic syndrome characterized by anorexia, body weight loss, loss of adipose tissue and skeletal muscle, accounting for at least 20% of deaths in neoplastic patients. CC significantly impairs quality of life and response to anti-neoplastic therapies, increasing morbidity and mortality of cancer patients. Muscle wasting is the most important phenotypic feature of CC and the principal cause of function impairment, fatigue and respiratory complications, mainly related to a hyperactivation of muscle proteolytic pathways. Most current therapeutic strategies to counteract CC have proven to be only partially effective. In the last decade, the correction of anorexia, the inhibition of catabolic processes and the stimulation of anabolic pathways in muscle have been attempted pharmacologically with encouraging results in animal models and through preliminary clinical trials. However, data in the clinical setting are still scanty and non definitive. It is time to start prospective, randomized, controlled trials to evaluate which drugs are effective in counteracting the loss of lean of muscle mass and in improving nutritional status and quality of life in patients affected by cancer-related cachexia. .COPYRGT. 2006 Society of Surgical Oncology.

CONTROLLED TERM: Medical Descriptors:
adipose tissue
adrenal insufficiency: SI, side effect
alopecia: SI, side effect
anorexia: DT, drug therapy
article
biosynthesis
blood pressure
*cachexia: DM, disease management
*cachexia: DT, drug therapy
*cachexia: ET, etiology
*cancer cachexia: DM, disease management
*cancer cachexia: DT, drug therapy
*cancer cachexia: ET, etiology
cancer patient
cancer: DT, drug therapy
catabolism
clinical trial
combination chemotherapy
coordination disorder: SI, side effect
drowsiness: SI, side effect
drug effect
drug mechanism
drug safety
energy expenditure

energy metabolism
enteric feeding
experimental model
fatigue
fluid retention
functional disease
human
hyperglycemia: SI, side effect
impotence: SI, side effect
lung non small cell cancer: DT, drug therapy
monotherapy
muscle atrophy
nonhuman
nutritional status
*paraneoplastic syndrome: DM, disease management
*paraneoplastic syndrome: DT, drug therapy
*paraneoplastic syndrome: ET, etiology
parenteral nutrition
peripheral edema: SI, side effect
phenotype
physical activity
protein degradation
pulse pressure
quality of life
respiratory tract disease
side effect: SI, side effect
skeletal muscle
thinking impairment: SI, side effect
thromboembolism: SI, side effect
vomiting: SI, side effect
weight reduction

CONTROLLED TERM: Drug Descriptors:
cannabis derivative: PD, pharmacology
cyclooxygenase 2 inhibitor: PD, pharmacology
cytokine antibody: DT, drug therapy
cytokine antibody: PD, pharmacology
cytokine
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: PD, pharmacology
docetaxel: CB, drug combination
docetaxel: DT, drug therapy
dronabinol: AE, adverse drug reaction
dronabinol: CT, clinical trial
dronabinol: CM, drug comparison
dronabinol: DT, drug therapy
dronabinol: PD, pharmacology
etanercept: CB, drug combination
etanercept: DT, drug therapy
fish oil: CB, drug combination
fish oil: DT, drug therapy
ghrelin: AE, adverse drug reaction
ghrelin: CT, clinical trial
ghrelin: DT, drug therapy
ghrelin: PD, pharmacology
ghrelin: SC, subcutaneous drug administration
hormone receptor blocking agent: DT, drug therapy
hormone receptor blocking agent: PD, pharmacology
ibuprofen: CB, drug combination
ibuprofen: DT, drug therapy
icosapentaenoic acid: CT, clinical trial

icosapentaenoic acid: CM, drug comparison
icosapentaenoic acid: DO, drug dose
icosapentaenoic acid: DT, drug therapy
icosapentaenoic acid: PO, oral drug administration
icosapentaenoic acid: PD, pharmacology
infliximab: CB, drug combination
infliximab: DT, drug therapy
interleukin 12: PD, pharmacology
interleukin 15: PD, pharmacology
megestrol acetate: AE, adverse drug reaction
megestrol acetate: CT, clinical trial
megestrol acetate: CB, drug combination
megestrol acetate: CM, drug comparison
megestrol acetate: DT, drug therapy
megestrol acetate: PD, pharmacology
melanocortin receptor antagonist: DT, drug therapy
melanocortin receptor antagonist: PD, pharmacology
melatonin: CT, clinical trial
melatonin: CB, drug combination
melatonin: DT, drug therapy
melatonin: PO, oral drug administration
melatonin: PD, pharmacology
myostatin antibody: DT, drug therapy
myostatin antibody: IP, intraperitoneal drug administration
myostatin antibody: PD, pharmacology
myostatin
n acetyl alpha intermedin[4-10]cyclo[4 norleucine 5 aspartic acid 7 [3 (2 naphthyl)alanine] 10 lysinamide]: DT, drug therapy
n acetyl alpha intermedin[4-10]cyclo[4 norleucine 5 aspartic acid 7 [3 (2 naphthyl)alanine] 10 lysinamide]: PD, pharmacology
nandrolone decanoate: CT, clinical trial
nandrolone decanoate: DT, drug therapy
nandrolone decanoate: IM, intramuscular drug administration
nandrolone decanoate: PD, pharmacology
oxandrolone: CT, clinical trial
oxandrolone: DT, drug therapy
oxandrolone: PD, pharmacology
pentoxifylline: CT, clinical trial
pentoxifylline: DT, drug therapy
pentoxifylline: PD, pharmacology
placebo
protein antibody: DT, drug therapy
protein antibody: PD, pharmacology
suramin: PD, pharmacology
thalidomide: CT, clinical trial
thalidomide: DT, drug therapy
thalidomide: PD, pharmacology

CAS REGISTRY NO.: (cannabis derivative) 38458-58-1; (docetaxel) 114977-28-5; (dronabinol) 7663-50-5; (etanercept) 185243-69-0, 200013-86-1; (fish oil) 8016-13-5; (ghrelin) 258279-04-8, 304853-26-7; (ibuprofen) 15687-27-1; (icosapentaenoic acid) 25378-27-2, 32839-30-8; (infliximab) 170277-31-3; (interleukin 12) 138415-13-1; (megestrol acetate) 595-33-5; (melatonin) 73-31-4; (myostatin) 197731-05-8; (n acetyl alpha intermedin[4-10]cyclo[4 norleucine 5 aspartic acid 7 [3 (2 naphthyl)alanine] 10 lysinamide]) 168482-23-3; (nandrolone decanoate) 360-70-3; (oxandrolone) 53-39-4; (pentoxifylline) 6493-05-6; (suramin) 129-46-4, 145-63-1;

(thalidomide) 50-35-1
CHEMICAL NAME: Shu 9119

L99 ANSWER 57 OF 66 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006380243 EMBASE Full-text
TITLE: Ghrelin and neurohumoral antagonists in the treatment of Cachexia associated with cardiopulmonary disease.
AUTHOR: Lainscak M.; Andreas S.; Scanlon P.D.; Somers V.K.; Anker S.D.
CORPORATE SOURCE: M. Lainscak, Department of Internal Medicine, General Hospital Murska Sobota, Vrbnjaka 6, SI-9000 Murska Sobota, Slovenia
SOURCE: Internal Medicine, (1 Aug 2006) Vol. 45, No. 13, pp. 837.
Refs: 5
ISSN: 0918-2918 E-ISSN: 1349-7235 CODEN: IEDIEP
COUNTRY: Japan
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 006 Internal Medicine
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Aug 2006
Last Updated on STN: 31 Aug 2006
CONTROLLED TERM: Medical Descriptors:
*cachexia: DI, diagnosis
*cachexia: DT, drug therapy
heart disease: DT, drug therapy
lung disease
prognosis
chronic disease
heart failure: DT, drug therapy
chronic obstructive lung disease
body composition
muscle atrophy
functional status
pathophysiology
human
letter
CONTROLLED TERM: Drug Descriptors:
*ghrelin: DT, drug therapy
neurohormone: EC, endogenous compound
hormone antagonist: DT, drug therapy
neurohormone antagonist: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
beta adrenergic receptor blocking agent: TO, drug toxicity
unclassified drug
CAS REGISTRY NO.: (ghrelin) 258279-04-8, 304853-26-7

L99 ANSWER 58 OF 66 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006041505 EMBASE Full-text
TITLE: Prescription for patients with chronic obstructive pulmonary disease: Gain weight.
AUTHOR: Spiegler P.
SOURCE: Clinical Pulmonary Medicine, (2006) Vol. 13, No. 1, pp. 69.
ISSN: 1068-0640 CODEN: CPMEF2
COUNTRY: United States
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis

030 Pharmacology
037 Drug Literature Index
006 Internal Medicine
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Feb 2006
Last Updated on STN: 6 Sep 2007
CONTROLLED TERM: Medical Descriptors:
*cachexia: DT, drug therapy
*chronic obstructive lung disease
clinical article
clinical trial
controlled clinical trial
controlled study
disease association
drug infusion
drug tolerability
food intake
grip strength
growth hormone blood level
hand grip
human
lean body weight
lung function
lung pressure
muscle strength
noradrenalin blood level
note
open study
performance
physical capacity
prescription
statistical significance
walking
*weight gain
CONTROLLED TERM: Drug Descriptors:
*ghrelin: CT, clinical trial
*ghrelin: DT, drug therapy
*ghrelin: IV, intravenous drug administration
*ghrelin: PD, pharmacology
glucose: EC, endogenous compound
growth hormone: EC, endogenous compound
hydrocortisone: EC, endogenous compound
insulin: EC, endogenous compound
interleukin 6: EC, endogenous compound
noradrenalin: EC, endogenous compound
tumor necrosis factor alpha: EC, endogenous compound
CAS REGISTRY NO.: (ghrelin) 258279-04-8, 304853-26-7; (glucose) 50-99-7, 84778-64-3; (growth hormone) 36992-73-1, 37267-05-3, 66419-50-9, 9002-72-6; (hydrocortisone) 50-23-7; (insulin) 9004-10-8; (noradrenalin) 1407-84-7, 51-41-2

L99 ANSWER 59 OF 66 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005421163 EMBASE Full-text
TITLE: Ghrelin, diet, and pulmonary function.
AUTHOR: Zaloga G.P.
CORPORATE SOURCE: Dr. G.P. Zaloga, Methodist Research Institute, Wile Hall, 1812 N Capitol Ave, Indianapolis, IN 46202, United States. gzaloga@clarian.org
SOURCE: Chest, (2005) Vol. 128, No. 3, pp. 1084-1086.

Refs: 16
ISSN: 0012-3692 CODEN: CHETBF
COUNTRY: United States
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Oct 2005
Last Updated on STN: 20 Oct 2005
CONTROLLED TERM: Medical Descriptors:
*chronic obstructive lung disease
*pulmonary hypertension
*cachexia: DT, drug therapy
protein function
protein synthesis
enterochromaffin cell
protein secretion
food intake
satiety
hypothalamus
protein expression
body mass
drug effect
lung function
dietary intake
appetite
human
clinical trial
editorial
priority journal
Drug Descriptors:
*ghrelin: CT, clinical trial
*ghrelin: DT, drug therapy
*ghrelin: EC, endogenous compound
*ghrelin: IV, intravenous drug administration
neuropeptide Y: EC, endogenous compound
cefquinome: EC, endogenous compound
noradrenalin: EC, endogenous compound
CAS REGISTRY NO.: (ghrelin) 258279-04-8, 304853-26-7; (neuropeptide Y) 82785-45-3, 83589-17-7; (cefquinome) 84957-30-2; (noradrenalin) 1407-84-7, 51-41-2

L99 ANSWER 60 OF 66 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005057323 EMBASE Full-text
TITLE: Ghrelin: More than a natural GH secretagogue and/or an orexigenic factor.
AUTHOR: Ghigo E.; Broglio F.; Arvat E.; Maccario M.; Papotti M.; Muccioli G.
CORPORATE SOURCE: E. Ghigo, Div. of Endocrinology and Metabolism, Department of Internal Medicine, University of Turin, C.so Dogliotti 14, 10126 Torino, Italy. ezio.ghigo@unito.it
SOURCE: Clinical Endocrinology, (2005) Vol. 62, No. 1, pp. 1-17. .
Refs: 273
ISSN: 0300-0664 CODEN: CLENAO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 18 Feb 2005
Last Updated on STN: 18 Feb 2005
ABSTRACT: Ghrelin, an acylated peptide produced predominantly by the stomach, has been discovered to be a natural ligand of the growth hormone secretagogue receptor type 1a (GHS-R1a). Ghrelin has recently attracted considerable interest as a new orexigenic factor. However, ghrelin exerts several other neuroendocrine, metabolic and also non-endocrine actions that are explained by the widespread distribution of ghrelin and GHS-R expression. The likely existence of GHS-R sub-types and evidence that the neuroendocrine actions, but not all the other actions, of ghrelin depend on its acylation in serine-3 revealed a system whose complexity had not been completely explored by studying synthetic GHS. Ghrelin secretion is mainly regulated by metabolic signals and, in turn, the modulatory action of ghrelin on the control of food intake and energy metabolism seems to be among its most important biological actions. However, according to a recent study, ghrelin-null mice are neither anorectics nor dwarfs and this evidence clearly depicts a remarkable difference from leptin null mice. Nevertheless, the original and fascinating story of ghrelin, as well as its potential pathophysiological implications in endocrinology and internal medicine, is not definitively cancelled by these data as GHS-R1a null aged mice show significant alterations in body composition and growth, in glucose metabolism, cardiac function and contextual memory. Besides potential clinical implications for natural or synthetic ghrelin analogues acting as agonists or antagonists, there are several open questions awaiting an answer. How many ghrelin receptor subtypes exist? Is ghrelin 'the' or just 'a' GHS-R ligand? That is, are there other natural GHS-R ligands? Is there a functional balance between acylated and unacylated ghrelin forms, potentially with different actions? Within the next few years suitable answers to these questions will probably be found, making it possible to gain a better knowledge of ghrelin's potential clinical perspectives.

CONTROLLED TERM: Medical Descriptors:
*hormone action
hormone synthesis
hormone structure
stomach
neuroendocrine system
hypothalamus hypophysis system
gonadotropin secreting cell
sleep
anxiety
metabolism
tissue distribution
gene expression
acylation
hormone release
regulatory mechanism
food intake
energy metabolism
pancreas islet
adipose tissue
liver
gonad
adrenal gland
thyroid gland
digestive system
knockout mouse
aging
body composition

growth
glucose metabolism
heart function
memory
contextual memory
cell proliferation
clinical medicine
growth hormone deficiency: DI, diagnosis
cachexia: TH, therapy
eating disorder: TH, therapy
obesity: ET, etiology
obesity: TH, therapy
human
nonhuman
review
priority journal
Drug Descriptors:
*ghrelin
*growth hormone secretagogue
*appetite stimulant
peptide hormone
ligand
growth hormone secretagogue receptor
receptor subtype
growth hormone secretagogue receptor 1a
serine
hormone derivative
ghrelin derivative
leptin
prolactin
corticotropin
unclassified drug

CAS REGISTRY NO.: (ghrelin) 258279-04-8, 304853-26-7; (serine) 56-45-1, 6898-95-9; (prolactin) 12585-34-1, 50647-00-2, 9002-62-4; (corticotropin) 11136-52-0, 9002-60-2, 9061-27-2

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ACCESSION NUMBER: 2004248737 EMBASE Full-text
TITLE: Is there a role of ghrelin in preventing catabolism?.
AUTHOR: Janssen J.A.M.J.L.; van der Lely A.J.; Lamberts S.W.J.
CORPORATE SOURCE: Dr. J.A.M.J.L. Janssen, Dept. of Internal Medicine, Erasmus MC, Dr Molewaterplein 40, 3000 CA Rotterdam, Netherlands. j.a.m.j.l.janssen@erasmusmc.nl
SOURCE: Journal of Endocrinological Investigation, (2004) Vol. 27, No. 4, pp. 400-403. .
Refs: 23
ISSN: 0391-4097 CODEN: JEIND7
COUNTRY: Italy
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 003 Endocrinology
016 Cancer
017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 28 Jun 2004
Last Updated on STN: 28 Jun 2004
ABSTRACT: Catabolism is a metabolic process in which muscle and fat cell tissues

are broken down in their constituent parts to provide nutrients and energy for the body. Whilst undoubtedly a potent stimulator of GH secretion in pharmacological doses, at present no clear physiological role for ghrelin in the regulation of GH secretion has been identified in man. In addition to its GH-releasing properties, ghrelin stimulates food intake and adipogenesis. The role of ghrelin has been extensively studied in three human models of catabolism: anorexia nervosa, cardiac cachexia and cancer cachexia. In this review we discuss the role of ghrelin in the etiology and treatment of catabolism using these three human models of catabolism. In the presence of clear catabolism in all the three conditions plasma total ghrelin levels are increased, suggesting that ghrelin does not increase food intake and/or anabolism in these circumstances. In addition, it is at present unknown whether administration of additional ghrelin in these conditions may reduce (or attenuate) the development of cachexia. In conclusion, the anabolic effects of ghrelin in man have still to be demonstrated. .COPYRGT. 2004, Editrice Kurtis.

CONTROLLED TERM: Medical Descriptors:
*anorexia nervosa: DT, drug therapy
*anorexia nervosa: ET, etiology
*anorexia nervosa: PC, prevention
*cachexia: CO, complication
*cachexia: DT, drug therapy
*cachexia: ET, etiology
*cachexia: PC, prevention
catabolism
muscle cell
adipocyte
nutrient supply
growth hormone release
food intake
lipogenesis
disease model
biosynthesis
pathogenesis
diet restriction
wasting syndrome: CO, complication
wasting syndrome: DT, drug therapy
wasting syndrome: ET, etiology
wasting syndrome: PC, prevention
heart failure
malignant neoplastic disease
human
nonhuman
rat
controlled study
short survey
Drug Descriptors:
*ghrelin: DT, drug therapy
*ghrelin: EC, endogenous compound
growth hormone: EC, endogenous compound
leptin: EC, endogenous compound
placebo

CAS REGISTRY NO.: (ghrelin) 258279-04-8, 304853-26-7; (growth hormone) 36992-73-1, 37267-05-3, 66419-50-9, 9002-72-6

L99 ANSWER 62 OF 66 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005042586 EMBASE Full-text
TITLE: GHRH and GH secretagogues: Clinical perspectives and safety.

AUTHOR: Aimaretti G.; Baldelli R.; Corneli G.; Bellone S.; Rovere S.; Croce C.; Ragazzoni F.; Giordano R.; Arvat E.; Bona G.; Ghigo E.
CORPORATE SOURCE: Dr. E. Ghigo, Div. of Endocrinology and Metabolism, Department of Internal Medicine, University of Turin, C.so Dogliotti 14, 10126 Torino, Italy. ezio.ghigo@unito.it
SOURCE: Pediatric Endocrinology Reviews, (2004) Vol. 2, No. SUPPL. 1, pp. 86-92. .
Refs: 51
ISSN: 1565-4753
COUNTRY: Israel
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
007 Pediatrics and Pediatric Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 10 Feb 2005
Last Updated on STN: 10 Feb 2005

ABSTRACT: The diagnosis and treatment of growth hormone deficiency (GHD), as well as the possibility of counteracting somatopause and age-related changes in body composition, structural functions, and metabolism, prompted interest in potential clinical uses of GH-releasing hormone (GHRH) and GH secretagogues (GHS). GHD often reflects hypothalamic GHRH deficiency and it has been clearly demonstrated that the age-related decline in the function of the GH/IGF-I axis reflects a reduction in hypothalamic function as evidenced by the preservation of the releasable pool of pituitary GH in aged subjects. The effectiveness of recombinant human GH (rhGH) is well established, but it is also recognized that GH replacement does not mimic physiological GH secretion which theoretically would be restored by GHRH and/or GHS. At present, it has been clearly demonstrated that GHRH and/or GHS represent reliable tools for the diagnosis of GHD. On the other hand, neither GHRH nor GHS has been shown to provide effective alternatives to rhGH for the treatment of GHD. Although GHRH and/or GHS represent the most logical approaches for the restoration of the GH/IGF-I axis to a youthful level of activity and for counteracting the somatopause, this hypothesis has never been proven definitively. Conceptually, GHRH replacement would be the most physiological approach and its safety is guaranteed, provided an appropriate dose is used, in order to avoid hyperactivity of the GH/IGF-I axis. However, a long-acting preparation is needed. On the other hand, GHS, e.g., ghrelin analogues, could be considered as a function of their selectivity of action. However, ghrelin has a wide spectrum of endocrine and non-endocrine actions at both central and peripheral levels. Thus, non-selective GHS, although available in orally active forms, could elicit unforeseen side effects. Previous studies with GHRH and/or GHS in aging patients provided encouraging results. However, it still remains to be definitively demonstrated that aged subjects would benefit from chronic treatment with these molecules.

CONTROLLED TERM: Medical Descriptors:
*growth hormone deficiency: DI, diagnosis
*growth hormone deficiency: DT, drug therapy
*growth hormone deficiency: ET, etiology
childhood disease: DI, diagnosis
childhood disease: DT, drug therapy
adult disease: DI, diagnosis
adult disease: DT, drug therapy
drug safety
hormone response
growth hormone release

aging
geriatric disorder: DT, drug therapy
somatopause: DT, drug therapy
drug mechanism
provocation test
somatic cell
insulin tolerance test
drug bioavailability
drug potentiation
drug effect
postmenopause osteoporosis: DT, drug therapy
fluid retention
side effect: SI, side effect
carpal tunnel syndrome: SI, side effect
hyperglycemia: SI, side effect
metabolic disorder: SI, side effect
human
nonhuman
clinical trial
child
review
Drug Descriptors:
*growth hormone releasing factor: AE, adverse drug reaction
*growth hormone releasing factor: CT, clinical trial
*growth hormone releasing factor: CB, drug combination
*growth hormone releasing factor: IT, drug interaction
*growth hormone releasing factor: DT, drug therapy
*growth hormone releasing factor: PK, pharmacokinetics
*growth hormone releasing factor: PD, pharmacology
*growth hormone releasing factor: IV, intravenous drug administration
*growth hormone releasing factor: PO, oral drug administration
*growth hormone releasing factor: PA, parenteral drug administration
*growth hormone releasing factor: SC, subcutaneous drug administration
*growth hormone secretagogue: AE, adverse drug reaction
*growth hormone secretagogue: CB, drug combination
*growth hormone secretagogue: IT, drug interaction
*growth hormone secretagogue: DT, drug therapy
*growth hormone secretagogue: PD, pharmacology
*growth hormone secretagogue: IV, intravenous drug administration
*growth hormone secretagogue: PO, oral drug administration
ghrelin: CB, drug combination
ghrelin: PD, pharmacology
ghrelin: IV, intravenous drug administration
ghrelin derivative: CB, drug combination
ghrelin derivative: PD, pharmacology
ghrelin derivative: IV, intravenous drug administration
ghrelin derivative: PO, oral drug administration
arginine: CB, drug combination
arginine: PD, pharmacology
arginine: IV, intravenous drug administration
pyridostigmine: CB, drug combination
pyridostigmine: PD, pharmacology
pyridostigmine: PO, oral drug administration
propranolol: CB, drug combination

propranolol: PD, pharmacology
galanin: CB, drug combination
galanin: PD, pharmacology
histidyl dextro tryptophylalanyltryptophyl dextro phenylalanyllysinamide: CB, drug combination
histidyl dextro tryptophylalanyltryptophyl dextro phenylalanyllysinamide: PD, pharmacology
histidyl dextro tryptophylalanyltryptophyl dextro phenylalanyllysinamide: IV, intravenous drug administration
growth hormone
somatomedin C
somatomedin binding protein 3
recombinant growth hormone: DT, drug therapy
ibutamoren: CT, clinical trial
ibutamoren: DO, drug dose
ibutamoren: PK, pharmacokinetics
ibutamoren: PD, pharmacology
ibutamoren: PO, oral drug administration
growth hormone releasing factor[1-29]: AE, adverse drug reaction
growth hormone releasing factor[1-29]: CT, clinical trial
growth hormone releasing factor[1-29]: CB, drug combination
growth hormone releasing factor[1-29]: DT, drug therapy
growth hormone releasing factor[1-29]: PD, pharmacology
growth hormone releasing factor[1-29]: IV, intravenous drug administration
growth hormone releasing factor[1-29]: SC, subcutaneous drug administration
growth hormone releasing hormone derivative: PD, pharmacology
growth hormone releasing hormone derivative: SC, subcutaneous drug administration
alendronic acid: CT, clinical trial
alendronic acid: CB, drug combination
alendronic acid: DT, drug therapy
alendronic acid: PD, pharmacology
unclassified drug

CAS REGISTRY NO.: (growth hormone releasing factor) 83930-13-6, 9034-39-3; (ghrelin) 258279-04-8, 304853-26-7; (arginine) 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3; (pyridostigmine) 101-26-8, 155-97-5; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (galanin) 88813-36-9; (histidyl dextro tryptophylalanyltryptophyl dextro phenylalanyllysinamide) 87616-84-0; (growth hormone) 36992-73-1, 37267-05-3, 66419-50-9, 9002-72-6; (somatomedin C) 67763-96-6; (ibutamoren) 159752-10-0; (growth hormone releasing factor[1-29]) 90830-28-7; (alendronic acid) 66376-36-1

CHEMICAL NAME: Mk 0677

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ACCESSION NUMBER: 2003330461 EMBASE Full-text

TITLE: Patent developments in anabolic agents for treatment of bone diseases.

AUTHOR: Wos J.A.; Lundy M.W.

CORPORATE SOURCE: J.A. Wos, Procter and Gamble Pharmaceuticals, 8700 Mason-Montgomery Road, Mason, OH 45040-8006, United States. wos.ja@pg.com

SOURCE: Expert Opinion on Therapeutic Patents, (1 Aug 2003) Vol. 13, No. 8, pp. 1141-1156. .

Refs: 70
ISSN: 1354-3776 CODEN: EOTPEG

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 030 Pharmacology
031 Arthritis and Rheumatism
033 Orthopedic Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 4 Sep 2003
Last Updated on STN: 4 Sep 2003

ABSTRACT: A review of the patent literature encompassing the past 3 years (.apprx. 2000-2003) in the area of bone anabolic therapies for treatment of osteoporosis and related diseases is described. A variety of potential therapeutics are covered, as well as improvement attempts on the first approved bone anabolic agent, recombinant human parathyroid hormone (rPrTH; teriparatide, Forteo®, Eli Lilly & Co.). The patent literature suggests that multiple strategies are currently being pursued in order to deliver the first orally bioavailable anabolic agent to the market and that a variety of new targets are also being evaluated for further development.

CONTROLLED TERM: Medical Descriptors:
*metabolic bone disease: DT, drug therapy
*metabolic bone disease: SI, side effect
*osteoporosis: DT, drug therapy
patent
drug approval
drug delivery system
drug marketing
drug targeting
drug efficacy
hypercalcemia: SI, side effect
osteosarcoma: SI, side effect
drug structure
drug half life
human
clinical trial
review

CONTROLLED TERM: Drug Descriptors:
*anabolic agent: AE, adverse drug reaction
*anabolic agent: CT, clinical trial
*anabolic agent: AD, drug administration
*anabolic agent: AN, drug analysis
*anabolic agent: CB, drug combination
*anabolic agent: CM, drug comparison
*anabolic agent: DV, drug development
*anabolic agent: DT, drug therapy
*anabolic agent: PR, pharmaceutics
*anabolic agent: PK, pharmacokinetics
*anabolic agent: PD, pharmacology
*anabolic agent: IH, inhalational drug administration
*anabolic agent: PO, oral drug administration
*anabolic agent: SC, subcutaneous drug administration
recombinant human parathyroid hormone: AE, adverse drug reaction
recombinant human parathyroid hormone: AD, drug administration

recombinant human parathyroid hormone: DT, drug therapy
recombinant human parathyroid hormone: PR, pharmaceutics
recombinant human parathyroid hormone: SC, subcutaneous drug administration
parathyroid hormone: AE, adverse drug reaction
parathyroid hormone: CT, clinical trial
parathyroid hormone: AD, drug administration
parathyroid hormone: CB, drug combination
parathyroid hormone: CM, drug comparison
parathyroid hormone: DT, drug therapy
parathyroid hormone: EC, endogenous compound
parathyroid hormone: PR, pharmaceutics
parathyroid hormone: PK, pharmacokinetics
parathyroid hormone: PD, pharmacology
parathyroid hormone: IH, inhalational drug administration
parathyroid hormone: PO, oral drug administration
parathyroid hormone: SC, subcutaneous drug administration
parathyroid hormone[1-34]: AE, adverse drug reaction
parathyroid hormone[1-34]: AD, drug administration
parathyroid hormone[1-34]: DT, drug therapy
parathyroid hormone[1-34]: PR, pharmaceutics
parathyroid hormone[1-34]: SC, subcutaneous drug administration
bisphosphonic acid derivative: CB, drug combination
bisphosphonic acid derivative: DT, drug therapy
bisphosphonic acid derivative: PD, pharmacology
alendronic acid: CB, drug combination
alendronic acid: DT, drug therapy
alendronic acid: PD, pharmacology
risedronic acid: CB, drug combination
risedronic acid: DT, drug therapy
risedronic acid: PD, pharmacology
parathyroid hormone related protein: AE, adverse drug reaction
parathyroid hormone related protein: CM, drug comparison
parathyroid hormone related protein: DT, drug therapy
parathyroid hormone related protein: PR, pharmaceutics
parathyroid hormone related protein: PD, pharmacology
parathyroid hormone derivative: AE, adverse drug reaction
parathyroid hormone derivative: CT, clinical trial
parathyroid hormone derivative: AD, drug administration
parathyroid hormone derivative: CB, drug combination
parathyroid hormone derivative: CM, drug comparison
parathyroid hormone derivative: DT, drug therapy
parathyroid hormone derivative: PR, pharmaceutics
parathyroid hormone derivative: PK, pharmacokinetics
parathyroid hormone derivative: PD, pharmacology
parathyroid hormone derivative: IH, inhalational drug administration
parathyroid hormone derivative: PO, oral drug administration
parathyroid hormone derivative: SC, subcutaneous drug administration
parathyroid hormone[1-84]: AE, adverse drug reaction
parathyroid hormone[1-84]: CT, clinical trial
parathyroid hormone[1-84]: AD, drug administration
parathyroid hormone[1-84]: CM, drug comparison
parathyroid hormone[1-84]: DT, drug therapy
parathyroid hormone[1-84]: PK, pharmacokinetics
parathyroid hormone[1-84]: PD, pharmacology

parathyroid hormone[1-84]: SC, subcutaneous drug administration
calcium antagonist: AN, drug analysis
calcium antagonist: CB, drug combination
calcium antagonist: DT, drug therapy
calcium antagonist: PD, pharmacology
2 chloro 6 [3 [1,1 dimethyl 2 (2 naphthyl)ethylamino] 2 hydroxypropoxy]benzonitrile: AN, drug analysis
2 chloro 6 [3 [1,1 dimethyl 2 (2 naphthyl)ethylamino] 2 hydroxypropoxy]benzonitrile: CB, drug combination
2 chloro 6 [3 [1,1 dimethyl 2 (2 naphthyl)ethylamino] 2 hydroxypropoxy]benzonitrile: DT, drug therapy
2 chloro 6 [3 [1,1 dimethyl 2 (2 naphthyl)ethylamino] 2 hydroxypropoxy]benzonitrile: PD, pharmacology
estrogen: CB, drug combination
estrogen: DT, drug therapy
estrogen: PD, pharmacology
growth hormone: EC, endogenous compound
growth hormone receptor: EC, endogenous compound
recombinant growth hormone: DT, drug therapy
recombinant growth hormone: SC, subcutaneous drug administration
prednisone: AE, adverse drug reaction
prednisone: PO, oral drug administration
glucocorticoid: AE, adverse drug reaction
glucocorticoid: PO, oral drug administration
growth hormone secretagogue: DT, drug therapy
growth hormone secretagogue: PD, pharmacology
  ghrelin derivative: DV, drug development
  ghrelin derivative: DT, drug therapy
  ghrelin derivative: PD, pharmacology
ghrelin: DV, drug development
ghrelin: DT, drug therapy
ghrelin: PD, pharmacology
ibutamoren: AN, drug analysis
ibutamoren: DV, drug development
ibutamoren: DT, drug therapy
ibutamoren: PD, pharmacology
ibutamoren: PO, oral drug administration
somatomedin: DV, drug development
somatomedin: DT, drug therapy
somatomedin: PD, pharmacology
vitamin D derivative: CT, clinical trial
vitamin D derivative: AN, drug analysis
vitamin D derivative: DV, drug development
vitamin D derivative: DT, drug therapy
vitamin D derivative: PD, pharmacology
hydroxymethylglutaryl coenzyme A reductase inhibitor: CT, clinical trial
hydroxymethylglutaryl coenzyme A reductase inhibitor: AN, drug analysis
hydroxymethylglutaryl coenzyme A reductase inhibitor: CB, drug combination
hydroxymethylglutaryl coenzyme A reductase inhibitor: DT, drug therapy
hydroxymethylglutaryl coenzyme A reductase inhibitor: PD, pharmacology
phosphodiesterase inhibitor: AN, drug analysis
phosphodiesterase inhibitor: DT, drug therapy
phosphodiesterase inhibitor: PD, pharmacology

prostaglandin derivative: AN, drug analysis
prostaglandin derivative: DT, drug therapy
prostaglandin derivative: PD, pharmacology
oxytocin: DT, drug therapy
oxytocin: PD, pharmacology
oxytocin derivative: DT, drug therapy
oxytocin derivative: PD, pharmacology
unindexed drug
unclassified drug
jtc 22

CAS REGISTRY NO.: (parathyroid hormone) 12584-96-2, 68893-82-3, 9002-64-6; (parathyroid hormone[1-34]) 12583-68-5, 52232-67-4; (alendronic acid) 66376-36-1; (risedronic acid) 105462-24-6, 122458-82-6; (2 chloro 6 [3 [1,1 dimethyl 2 (2 naphthyl)ethylamino] 2 hydroxypropoxy]benzonitrile) 284035-33-2, 324523-20-8; (growth hormone) 36992-73-1, 37267-05-3, 66419-50-9, 9002-72-6; (prednisone) 53-03-2; (ghrelin) 258279-04-8, 304853-26-7; (ibutamoren) 159752-10-0; (oxytocin) 50-56-6, 54577-94-5

CHEMICAL NAME: (1) Forteo; (2) Fosamax; (3) Actonel; (4) Nps 2143; (5) Jtc 22; (6) Mk 0677

COMPANY NAME: (1) Lilly; (2) Instituto Gentili; (3) Norwich Eaton; (4) NPS; (5) Japan Tobacco; (6) Merck; Tanabe; Ono; Procter and Gamble; Alcon; Allergan; Bristol Myers Squibb; Hoechst Marion Roussel; Bayer; Pfizer; Novartis

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ACCESSION NUMBER: 2003459309 EMBASE Full-text

TITLE: Ghrelin and the Endocrine Pancreas.

AUTHOR: Broglio F.; Gottero C.; Benso A.; Prodam F.; Volante M.; Destefanis S.; Gauna C.; Muccioli G.; Papotti M.; Van Der Lely A.J.; Ghigo E.

CORPORATE SOURCE: Dr. E. Ghigo, Div. of Endocrinology and Metabolism, Department of Internal Medicine, University of Turin, 14 10126 Turin, Italy. ezio.ghigo@unito.it

SOURCE: Endocrine, (2003) Vol. 22, No. 1, pp. 19-24. .
Refs: 61
ISSN: 0969-711X CODEN: EOCRE5

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 4 Dec 2003
Last Updated on STN: 4 Dec 2003

ABSTRACT: Ghrelin is a 28-amino-acid peptide predominantly produced by the stomach, while substantially lower amounts derive from other tissues including the pancreas. It is a natural ligand of the GH secretagogue (GHS) receptor (GHS-R1a) and strongly stimulates GH secretion, but acylation in serine 3 is needed for its activity. Ghrelin also possesses other endocrine and nonendocrine actions reflecting central and peripheral GHS-R distribution including the pancreas. The wide spectrum of ghrelin activities includes orexigenic effect, control of energy expenditure, and peripheral gastroenteropancreatic actions. Circulating ghrelin levels mostly reflect gastric secretion as indicated by evidence that they are reduced by 80% after gastrectomy and even after gastric by-pass surgery. Ghrelin secretion is

increased in anorexia and cachexia but reduced in obesity, a notable exception being Prader-Willi syndrome. The negative association between ghrelin secretion and body weight is emphasized by evidence that weight increase and decrease reduces and augments circulating ghrelin levels in anorexia and obesity, respectively, and agrees with the clear negative association between ghrelin and insulin levels. In fact, ghrelin secretion is increased by fasting whereas it is decreased by glucose load as well as during euglycemic clamp but not after arginine or free fatty acid load in normal subjects; in physiological conditions, however, the most remarkable inhibitory input on ghrelin secretion is represented by somatostatin as well as by its natural analog cortistatin that concomitantly reduce β-cell secretion. This evidence indicates that the endocrine pancreas plays a role in directly or indirectly modulating ghrelin secretion. As anticipated, ghrelin, in turn, is expressed within the endocrine pancreas, although it is still matter of debate if it is expressed by β-, α-, or non-α/non-β cells. Moreover, GHS-R1a expression in the pancreas has been demonstrated by many authors. Some impact of synthetic GHS on insulin secretion and glucose metabolism had been reported in both animal and human studies. Depending on dose and experimental conditions ghrelin has been shown able to inhibit or stimulate insulin secretion in animals. In humans, ghrelin administration is followed by transient inhibition of insulin levels that surprisingly follows persistent increase in plasma glucose levels suggesting that ghrelin would also directly or indirectly activate glycogenolisis. Current studies indicate that ghrelin also blunts the insulin response to arginine but not that to oral glucose load in humans. These acute effects of ghrelin are independent of any cholinergic mediation and are not shared by synthetic, peptidyl GHS indicating they are likely mediated by a non-GHS-R1a receptor. These acute effects of ghrelin on insulin secretion would be short-lasting, and it has to be remembered that long-term treatment with synthetic non peptidyl GHS in healthy elderly subjects was followed by insulin resistance. In all, it is already clear that ghrelin has remarkable impact in modulating insulin secretion and glucose metabolism. Insulin and ghrelin secretions seem linked by a negative functional relationship that strengthens the hypothesized role of ghrelin in participating in the management of the neuroendocrine and metabolic response to variations in energy balance.

CONTROLLED TERM: Medical Descriptors:
*hormone action
*pancreas function
hormone release
hormone synthesis
hormone receptor interaction
growth hormone release
acylation
protein modification
appetite
anorexia
hormone blood level
stomach secretion
gastrectomy
stomach bypass
stomach surgery
cachexia
obesity
Prader Willi syndrome
body weight
insulin blood level
diet restriction
glucose tolerance test
pancreas islet beta cell

protein expression
insulin release
glucose metabolism
glucose blood level
glycogenolysis
cholinergic activity
aging
energy balance
food intake
drug activity
human
nonhuman
review
priority journal
Drug Descriptors:
*ghrelin: EC, endogenous compound
*hormone derivative: DO, drug dose
*hormone derivative: PD, pharmacology
*hormone derivative: PO, oral drug administration
*ghrelin derivative: DO, drug dose
*ghrelin derivative: PD, pharmacology
*ghrelin derivative: PO, oral drug administration
growth hormone secretagogue receptor 1a: EC, endogenous compound
growth hormone secretagogue receptor: EC, endogenous compound
somatostatin
somatostatin derivative: PD, pharmacology
cortistatin: PD, pharmacology
growth hormone secretagogue: PD, pharmacology
growth hormone secretagogue: PO, oral drug administration
insulin: EC, endogenous compound
glucose: EC, endogenous compound
unclassified drug

CAS REGISTRY NO.: (ghrelin) 258279-04-8, 304853-26-7; (somatostatin) 38916-34-6, 51110-01-1; (insulin) 9004-10-8; (glucose) 50-99-7, 84778-64-3

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ACCESSION NUMBER: 2001350166 EMBASE Full-text
TITLE: Structural similarity of ghrelin derivatives to peptidyl growth hormone secretagogues.
AUTHOR: Matsumoto M.; Kitajima Y.; Iwanami T.; Hayashi Y.; Tanaka S.; Minamitake Y.; Hosoda H.; Kojima M.; Matsuo H.; Kangawa K.
CORPORATE SOURCE: Y. Minamitake, Suntory Inst. Med. Res. and Devt., 2716-1 Kurakake, Akaiwa, Ohra-gun, Gunma 370-0503, Japan. Yoshiharu_Minamitake@suntory.co.jp
SOURCE: Biochemical and Biophysical Research Communications, (2001) Vol. 284, No. 3, pp. 655-659. .
Refs: 12
ISSN: 0006-291X CODEN: BBRCA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 25 Oct 2001

Last Updated on STN: 25 Oct 2001

ABSTRACT: Ghrelin is a 28-amino acid residue endogenous growth hormone secretagogue. Intensive investigations revealed that the N-terminus tetrapeptide, having octanoyl group at Ser(3), is the minimum active core. In this study, we further explored the structure-function relationships of the active N-terminus portion of ghrelin using a Ca(2+) mobilization assay. The smallest and most potent ghrelin derivative we have found so far is 5-aminopentanoyl-Ser(Octyl)-Phe-Leu-aminoethylamide, showing comparable activity to the natural molecule. In the process of modifying the active core, the ghrelin-derived short analogues emerged structurally close to peptidyl growth hormone secretagogues. The N-terminus modification suggested that Gly(1)-Ser(2) unit works as a spacer, forming adequate distance between N(α)-amino group and n-octanoyl group. Replacement of 3rd and 4th amino acid residues to D-isomer suggested that the N-terminal dipeptide contributes to shape the biologically active geometry by effecting conformation of residues in positions 3 and 4. .COPYRGT. 2001 Academic Press.

CONTROLLED TERM: Medical Descriptors:
*growth hormone release
amino acid sequence
protein conformation
geometry
hormone structure
peptide synthesis
article
priority journal
Drug Descriptors:
*growth hormone
*ghrelin derivative
unclassified drug
CAS REGISTRY NO.: (growth hormone) 36992-73-1, 37267-05-3, 66419-50-9, 9002-72-6

L99 ANSWER 66 OF 66 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001019512 EMBASE Full-text
TITLE: Structure - Function studies on the new growth hormone-releasing peptide, ghrelin: Minimal sequence of ghrelin necessary for activation of growth hormone secretagogue receptor 1a.
AUTHOR: Bednarek M.A.; Feighner S.D.; Pong S.-S.; McKee K.K.; Hreniuk D.L.; Silva M.V.; Warren V.A.; Howard A.D.; Van der Ploeg L.H.Y.; Heck J.V.
CORPORATE SOURCE: M.A. Bednarek, Department of Medicinal Chemistry, Merck Research Laboratories, R50G-141, P.O. Box 2000, Rahway, NJ 07065, United States. maria_bednarek@merck.com
SOURCE: Journal of Medicinal Chemistry, (16 Nov 2000) Vol. 43, No. 23, pp. 4370-4376. .
Refs: 18
ISSN: 0022-2623 CODEN: JMCMAR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Feb 2001
Last Updated on STN: 1 Feb 2001

ABSTRACT: The recently discovered growth hormone secretagogue, ghrelin, is a potent agonist at the human growth hormone secretagogue receptor 1a (hGHSR1a).

To elucidate structural features of this peptide necessary for efficient binding to and activation of the receptor, several analogues of ghrelin with various aliphatic or aromatic groups in the side chain of residue 3, and several short peptides derived from ghrelin, were prepared and tested in a binding assay and in an assay measuring intracellular calcium elevation in HEK-293 cells expressing hGHSR1a. Bulky hydrophobic groups in the side chain of residue 3 turned out to be essential for maximum agonist activity. Also, short peptides encompassing the first 4 or 5 residues of ghrelin were found to functionally activate hGHSR1a about as efficiently as the full-length ghrelin. Thus the entire sequence of ghrelin is not necessary for activity: the Gly-Ser-Ser(n-octanoyl)-Phe segment appears to constitute the "active core" required for agonist potency at hGHSR1a.

CONTROLLED TERM: Medical Descriptors:
*structure activity relation
amino acid sequence
drug structure
drug activity
drug synthesis
drug receptor binding
assay
calcium cell level
human
controlled study
human cell
article
Drug Descriptors:
*growth hormone releasing factor derivative: AN, drug analysis
*growth hormone releasing factor derivative: CM, drug comparison
*growth hormone releasing factor derivative: DV, drug development
*growth hormone releasing factor derivative: PD, pharmacology
*ghrelin derivative: AN, drug analysis
*ghrelin derivative: CM, drug comparison
*ghrelin derivative: DV, drug development
*ghrelin derivative: PD, pharmacology
*growth hormone releasing factor receptor: EC, endogenous compound
calcium: EC, endogenous compound
pralmorelin: AN, drug analysis
pralmorelin: CM, drug comparison
pralmorelin: PD, pharmacology
growth hormone releasing peptide 1: AN, drug analysis
growth hormone releasing peptide 1: CM, drug comparison
growth hormone releasing peptide 1: PD, pharmacology
hexarelin: AN, drug analysis
hexarelin: CM, drug comparison
hexarelin: PD, pharmacology
ibutamoren: AN, drug analysis
ibutamoren: CM, drug comparison
ibutamoren: DV, drug development
ibutamoren: PD, pharmacology
unclassified drug

CAS REGISTRY NO.: (calcium) 7440-70-2; (pralmorelin) 158861-67-7; (hexarelin) 140703-51-1; (ibutamoren) 159752-10-0

CHEMICAL NAME: Mk 0677

FILE 'HOME' ENTERED AT 14:53:27 ON 20 SEP 2007

SEARCH HISTORY

=> d his nofile

(FILE 'HOME' ENTERED AT 13:57:23 ON 20 SEP 2007)

FILE 'CAPLUS' ENTERED AT 13:57:30 ON 20 SEP 2007
E US2006-567406/APPS
L1 1 SEA ABB=ON US2006-567406/AP
D SCAN
L2 608 SEA ABB=ON HOLST LANGE B?/AU OR LANGE B?/AU OR HOLST B?/AU
L3 1134 SEA ABB=ON HANSEN C?/AU
L4 1 SEA ABB=ON COPENHAGEN H?/AU
D SCAN L4
L5 471 SEA ABB=ON NILSSON H?/AU
L6 1 SEA ABB=ON L2 AND L3 AND (L4 OR L5)

FILE 'REGISTRY' ENTERED AT 13:59:56 ON 20 SEP 2007
L7 1 SEA ABB=ON 304853-26-7
D SCAN

FILE 'CAPLUS' ENTERED AT 14:00:10 ON 20 SEP 2007
L8 75 SEA ABB=ON L7/D
E CACHEXIA+ALL/CT
L9 3047 SEA ABB=ON CACHEXIA/OBI
L10 1571 SEA ABB=ON WASTING/OBI
L11 20291 SEA ABB=ON APPETITE/OBI
L12 5750 SEA ABB=ON MALNUTRITION/OBI
L13 23 SEA ABB=ON L8 AND (L9 OR L10 OR L11 OR L12)
L14 497406 SEA ABB=ON NEOPLAS?/OBI
L15 30 SEA ABB=ON L8 AND (L9 OR L10 OR L11 OR L12 OR L14)
L16 7 SEA ABB=ON L15 NOT L13
D SCAN TI
L17 29 SEA ABB=ON L8(L)(THU OR PAC OR PKT OR DMA)/RL
L18 2 SEA ABB=ON L8(L)BAC/RL
D SCAN
L19 27682 SEA ABB=ON BODY WEIGHT/CT
L20 35 SEA ABB=ON L8 AND ((L9 OR L10 OR L11 OR L12 OR L19) OR (L17 AND L14))
L21 5 SEA ABB=ON (L2 OR L3 OR L4 OR L5) AND L8
L22 5 SEA ABB=ON (L1 OR L21)
D AB L1
SEL RN L1

FILE 'REGISTRY' ENTERED AT 14:07:31 ON 20 SEP 2007
L23 84 SEA ABB=ON (304853-26-7/BI OR 258279-04-8/BI OR 307950-60-3/BI OR 313951-59-6/BI OR 321974-46-3/BI OR 321974-68-9/BI OR 57-88-5/BI OR 603973-45-1/BI OR 603973-46-2/BI OR 613670-28-3/BI OR 613670-31-8/BI OR 63-89-8/BI OR 67763-96-6/BI OR 843660-25-3/BI OR 845463-09-4/BI OR 845463-10-7/BI OR 845463-11-8/BI OR 845463-12-9/BI OR 845463-13-0/BI OR 845463-14-1/BI OR 845463-15-2/BI OR 845463-16-3/BI OR 845463-17-4/BI OR 845463-18-5/BI OR 845463-19-6/BI OR 845463-20-9/BI OR 845463-21-0/BI OR 845463-22-1/BI OR 845463-23-2/BI OR 845463-24-3/BI OR 845463-25-4/BI OR 845463-26-5/BI OR 845463-27-6/BI OR 845463-28-7/BI OR 845463-29-8/BI OR 845463-30-1/BI OR 845463-31-2/BI OR 845463-32-3/BI OR 845463-33-4/BI OR 845463-34-5/BI OR 845463-35-6/BI OR 845463-36-7/BI OR 845463-37-8/BI OR 845463-38-9/BI OR 845463-39-0/BI OR 845463-40-3/BI OR 845463-41-4/BI OR 845463-42-5/BI OR 845463-43-6/BI OR 845463-44-7/BI OR 845463-45-8/BI OR 845463-46-9/BI OR

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                845463-47-0/BI OR 845463-48-1/BI OR 845463-49-2/BI OR 845463-50
                -5/BI OR 845463-51-6/BI OR 845463-52-7/BI OR 845463-53-8/BI OR
                845463-54-9/BI OR 845463-55-0/BI OR 845463-56-1/BI OR 845463-57
                -2/BI OR 845463-58-3/BI OR 845463-59-4/BI OR 845463-60-7/BI OR
                845463-61-8/BI OR 845463-62-9/BI OR 845463-63-0/BI OR 845463-64
                -1/BI OR 845463-65-2/BI OR 845463-66-3/BI OR 845463-67-4/BI OR
                845463-68-5/BI OR 845463-69-6/BI OR 845463-70-9/BI OR 845463-71
                -0/BI OR 845463-72-1/BI OR 845463-73-2/BI OR 845463-74-3/BI OR
                845463-75-4/BI OR 845463-76-5/BI OR 845463-77-6/BI OR 845463-78
                -7/BI)
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 14:08:12 ON 20 SEP 2007

     FILE 'MEDLINE' ENTERED AT 14:10:04 ON 20 SEP 2007
L24          471 SEA ABB=ON  HOLST LANGE B?/AU OR LANGE B?/AU OR HOLST B?/AU
L25          845 SEA ABB=ON  HANSEN C?/AU
L26          300 SEA ABB=ON  COPENHAGEN H?/AU OR NILSSON H?/AU
L27            0 SEA ABB=ON  L24 AND L25 AND L26
L28         2304 SEA ABB=ON  GHRELIN
L29            0 SEA ABB=ON  PEPTIDE HORMONES/CT(L)AA/CT
L30         2202 SEA ABB=ON  PEPTIDE HORMONES/CT
L31        96078 SEA ABB=ON  PEPTIDES/CT
L32         2754 SEA ABB=ON  CACHEXIA/CT
L33          553 SEA ABB=ON  WASTING SYNDROME/CT
L34           34 SEA ABB=ON  L28 AND (L30 OR L31) AND (L32 OR L33)
                D TRIAL 1-5
L35         8287 SEA ABB=ON  EATING/CT(L)DE/CT
L36         4131 SEA ABB=ON  APPETITE/CT
L37          106 SEA ABB=ON  L30 AND PY<2002

     FILE 'STNGUIDE' ENTERED AT 14:15:03 ON 20 SEP 2007

     FILE 'MEDLINE' ENTERED AT 14:19:47 ON 20 SEP 2007
                D PY 106
L38           98 SEA ABB=ON  L28 AND L37
L39          526 SEA ABB=ON  L30(L)(AD OR PD OR TU OR PK)/CT
L40          124 SEA ABB=ON  L39 AND (L32 OR L33 OR L35 OR L36)
L41          121 SEA ABB=ON  L39 AND (L32 OR L33 OR L35 OR L36) AND L28
L42           13 SEA ABB=ON  L39 AND L32 AND L28
L43            9 SEA ABB=ON  (L24 OR L25 OR L26) AND L28
                D TRIAL 1-9
L44          351 SEA ABB=ON  L39/MAJ
L45          318 SEA ABB=ON  L44 AND L28
L46            1 SEA ABB=ON  L33 AND L45
L47           66 SEA ABB=ON  L35 AND L45
L48           20 SEA ABB=ON  L36 AND L45
L49            1 SEA ABB=ON  L28 AND L30 AND L33
L50       748646 SEA ABB=ON  NEOPLASMS+NT/CT(L)TH./CT
L51            1 SEA ABB=ON  (L35 OR L36) AND L45 AND L50
L52       725074 SEA ABB=ON  ANALOG? OR SECRETAGOG? OR DERIVATI?
L53           19 SEA ABB=ON  L28(W)LIKE
L54            1 SEA ABB=ON  L53 AND (L32 OR L33 OR L35 OR L36)
L55          642 SEA ABB=ON  L28 AND L30 AND L52
L56           47 SEA ABB=ON  L55 AND L39 AND (L32 OR L33 OR L35 OR L36)
                D KWIC 1-3
L57          195 SEA ABB=ON  L28(5A)L52
L58           16 SEA ABB=ON  L30 AND L57 AND (L32 OR L33 OR L35 OR L36)
                D TRIAL 1-16
                D QUE
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L59            6 SEA ABB=ON  L28(1A)L52 AND L30 AND (L32 OR L33 OR L35 OR L36)

     FILE 'EMBASE' ENTERED AT 14:32:16 ON 20 SEP 2007
                E GHRELIN/CT
                E E3+ALL
L60         2434 SEA ABB=ON  GHRELIN/CT
L61            7 SEA ABB=ON  GHRELIN DERIVATIVE/CT
                E GHRELIN DERIVATIVE/CT
L62          410 SEA ABB=ON  HOLST LANGE B?/AU OR LANGE B?/AU OR HOLST B?/AU
L63          638 SEA ABB=ON  HANSEN C?/AU
L64          259 SEA ABB=ON  COPENHAGEN H?/AU OR NILSSON H?/AU
L65            8 SEA ABB=ON  (L62 OR L63 OR L64) AND (L60 OR L61)
                D TRIAL L61 1-7
                E CACHEXIA/CT
                E E3+ALL
                E CANCER CACH/CT
L66           14 SEA ABB=ON  CANCER CACHEXIA/CT OR CANCER CACHEXIA SYNDROME/CT
L67         3660 SEA ABB=ON  CACHEXIA/CT
L68          109 SEA ABB=ON  L60 AND (L66 OR L67)
                D TRIAL 1-5
L69          459 SEA ABB=ON  L60(L)(AD OR DT OR PK OR DO OR PD)/CT
L70            3 SEA ABB=ON  L66 AND L60
L71          721 SEA ABB=ON  L67(L)(DT OR PC)/CT
L72           42 SEA ABB=ON  L69 AND L71
L73            8 SEA ABB=ON  L69/MAJ AND L71/MAJ

     FILE 'WPIX' ENTERED AT 14:37:23 ON 20 SEP 2007
L74          191 SEA ABB=ON  HOLST LANGE B?/AU OR LANGE B?/AU OR HOLST B?/AU
L75          453 SEA ABB=ON  HANSEN C?/AU
L76          157 SEA ABB=ON  COPENHAGEN H?/AU OR NILSSON H?/AU
L77            1 SEA ABB=ON  L74 AND L75 AND L76
                D TRIAL

     FILE 'STNGUIDE' ENTERED AT 14:37:58 ON 20 SEP 2007

     FILE 'LWPI' ENTERED AT 14:39:45 ON 20 SEP 2007
                E B04-B04D5+ALL/MC
                E B04-C01+ALL/MC
                E B04-H06+ALL/MC
                E B04-L04+ALL/MC
                E B11-C08E+ALL/MC
                E B12-K04A+ALL/MC E B12-M04+ALL/MC
                E B14-E11B+ALL/MC
                E B14-H01+ALL/MC
                E B14-L01+ALL/MC
                E S03-E14A1+ALL/MC
                E S03-E14H1+ALL/MC

     FILE 'STNGUIDE' ENTERED AT 14:39:57 ON 20 SEP 2007

     FILE 'LWPI' ENTERED AT 14:40:51 ON 20 SEP 2007
                E B12-K04A+ALL/MC
                E B12-M04+ALL/MC

     FILE 'STNGUIDE' ENTERED AT 14:40:54 ON 20 SEP 2007

     FILE 'WPIX' ENTERED AT 14:43:38 ON 20 SEP 2007
L78         94984 SEA ABB=ON  (B14-H01+NT/MC OR C14-H01+NT/MC OR B12-G07/MC OR
                C12-G07/MC)
L79          3107 SEA ABB=ON  CACHEXIA/BI,ABEX OR CACHECTIC?/BI,ABEX
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L80         570 SEA ABB=ON  B14-E11B/MC OR C14-E11B/MC
L81         212 SEA ABB=ON  GHRELIN/BI,ABEX
L82      542701 SEA ABB=ON  ANALOG?/BI,ABEX OR SECRETAGOG?/BI,ABEX OR DERIVATI?
                 /BI,ABEX
L83          25 SEA ABB=ON  (L79 OR L80) AND L81
L84          23 SEA ABB=ON  L81(1A)L82
L85          10 SEA ABB=ON  L84 AND (L79 OR L80)
L86          10 SEA ABB=ON  (L74 OR L75 OR L76) AND L81
L87           8 SEA ABB=ON  (L74 OR L75 OR L76) AND (L84 OR (L81 AND (L79 OR
                 L80)))
L88           8 SEA ABB=ON  (L87 OR L77)
L89           3 SEA ABB=ON  L85 AND L88

     FILE 'STNGUIDE' ENTERED AT 14:46:28 ON 20 SEP 2007

     FILE 'CAPLUS' ENTERED AT 14:49:01 ON 20 SEP 2007
               D QUE L22

     FILE 'MEDLINE' ENTERED AT 14:49:01 ON 20 SEP 2007
               D QUE L43

     FILE 'EMBASE' ENTERED AT 14:49:02 ON 20 SEP 2007
               D QUE L65

     FILE 'WPIX' ENTERED AT 14:49:02 ON 20 SEP 2007
               D QUE L88

     FILE 'MEDLINE, CAPLUS, WPIX, EMBASE' ENTERED AT 14:49:03 ON 20 SEP 2007
L90          18 DUP REM L43 L22 L88 L65 (12 DUPLICATES REMOVED)
                    ANSWERS '1-9' FROM FILE MEDLINE
                    ANSWERS '10-14' FROM FILE CAPLUS
                    ANSWERS '15-17' FROM FILE WPIX
                    ANSWER '18' FROM FILE EMBASE
               D IALL 1-9
               D IBIB AB HITIND 10-14
               D IALL ABEQ TECH 15-17
               D IALL 18

     FILE 'STNGUIDE' ENTERED AT 14:49:41 ON 20 SEP 2007

     FILE 'CAPLUS' ENTERED AT 14:50:53 ON 20 SEP 2007
               D QUE L20
L91          30 SEA ABB=ON  L20 NOT L22

     FILE 'MEDLINE' ENTERED AT 14:50:54 ON 20 SEP 2007
               D QUE L42
               D QUE L49
               D QUE L51
               D QUE L54
               D QUE L59
L92          21 SEA ABB=ON  (L42 OR L49 OR L51 OR L54 OR L59) NOT L43

     FILE 'EMBASE' ENTERED AT 14:50:56 ON 20 SEP 2007
               D QUE L61
               D QUE L70
               D QUE L73
L93           0 SEA ABB=ON  L61,L70,73 NOT L65

     FILE 'WPIX' ENTERED AT 14:50:58 ON 20 SEP 2007
               D QUE L85
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L94           7 SEA ABB=ON  L85 NOT L88

     FILE 'CAPLUS' ENTERED AT 14:52:05 ON 20 SEP 2007
               D QUE L20
L95          30 SEA ABB=ON  L20 NOT L22

     FILE 'MEDLINE' ENTERED AT 14:52:07 ON 20 SEP 2007
               D QUE L42
               D QUE L49
               D QUE L51
               D QUE L54
               D QUE L59
L96          21 SEA ABB=ON  (L42 OR L49 OR L51 OR L54 OR L59) NOT L43

     FILE 'EMBASE' ENTERED AT 14:52:09 ON 20 SEP 2007
               D QUE L61
               D QUE L70
               D QUE L73
L97          17 SEA ABB=ON  (L61 OR L70 OR L73) NOT L65

     FILE 'WPIX' ENTERED AT 14:52:10 ON 20 SEP 2007
               D QUE L85
L98           7 SEA ABB=ON  L85 NOT L88

     FILE 'STNGUIDE' ENTERED AT 14:52:22 ON 20 SEP 2007

     FILE 'MEDLINE, CAPLUS, WPIX, EMBASE' ENTERED AT 14:52:46 ON 20 SEP 2007
L99          66 DUP REM L96 L95 L98 L97 (9 DUPLICATES REMOVED)
                    ANSWERS '1-21' FROM FILE MEDLINE
                    ANSWERS '22-51' FROM FILE CAPLUS
                    ANSWERS '52-55' FROM FILE WPIX
                    ANSWERS '56-66' FROM FILE EMBASE
               D IALL 1-21
               D IBIB AB HITIND 22-51
               D IALL ABEQ TECH 52-55
               D IALL 56-66

     FILE 'HOME' ENTERED AT 14:53:27 ON 20 SEP 2007

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